Impact of baricitinib in combination with topical steroids on atopic dermatitis symptoms, quality of life and functioning in adult patients with moderate-to-severe atopic dermatitis from the BREEZE-AD7 Phase 3 randomized trial

A. Wollenberg,1 T. Nakahara,2 C. Maari,3 K. Peris,4 P. Lio,5 M. Augustin,6 J.I. Silverberg,7 M.J. Rueda,8* A.M. DeLozier,8 E. Pierce,8 F.E. Yang,8 L. Sun,8 S. Ball,8 M. Tauber,9 C. Paul9

1Department of Dermatology and Allergy, Ludwig Maximilian University, Munich, Germany
2Department of Dermatology, Kyushu University, Fukuoka, Japan
3Division of Dermatology, Innovaderm Research and Montreal University, Montreal, Quebec, Canada
4Dermatology, Università Cattolica del Sacro Cuore and Fondazione Policlinico Agostino Gemelli – IRCCS, Rome, Italy
5Northwestern University Feinberg School of Medicine, Chicago, IL, USA
6University Medical Center Hamburg-Eppendorf, Hamburg, Germany
7George Washington University School of Medicine and Health Sciences, Washington, DC, USA
8Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, USA
9Toulouse University and CHU Larrey, Toulouse, France

*Correspondence: M.J. Rueda. E-mail: rueda_maria_jose@lilly.com

Abstract

Background Baricitinib is an oral, selective, reversible Janus kinase 1/2 inhibitor approved in the European Union and Japan and under investigation in the United States for treatment of atopic dermatitis (AD).

Objectives To evaluate the impact of baricitinib plus background topical corticosteroids (TCS) on health-related quality of life (HRQoL), how AD symptoms impact work productivity and life functioning, and treatment benefit using patient-reported outcome (PRO) assessments in patients with moderate-to-severe AD previously experiencing inadequate response to TCS.

Methods Adult patients with AD in BREEZE-AD7, a Phase 3, multicentre, double-blind trial, were randomised 1 : 1 : 1 to daily oral placebo (control) or baricitinib 4- or 2-mg plus TCS. PROs reported Week 1 through Week 16: Dermatology Life Quality Index (DLQI), Work Productivity and Activity Impairment-AD (WPAI-AD); Patient-Reported Outcomes Measurement Information System (PROMIS) Itch and Sleep measures, and Patient Benefit Index (PBI). Data were analysed using logistic regression (categorical) and mixed model repeated measures (continuous). PBI scores were analysed using analysis of variance.

Results A total of 329 patients were randomised. Treatment with baricitinib 4-mg (N = 111) or 2 mg (N = 109) plus TCS led to rapid, statistically significant improvements [vs. TCS plus placebo (N = 109)] in DLQI ≥4-point improvement starting at Week 2 (4-mg plus TCS, P ≤ 0.001; 2-mg plus TCS P ≤ 0.05), change from baseline in WPAI-AD presenteeism at Week 1 (4-mg plus TCS, P ≤ 0.01; 2-mg plus TCS P ≤ 0.05) and PROMIS itch interference at Week 2 (4-mg plus TCS P ≤ 0.01). Improvements were sustained through Week 16 for baricitinib 4-mg. Statistically significant improvements were observed at Week 16 for PBI global score (4-mg plus TCS, P ≤ 0.001; 2-mg plus TCS P ≤ 0.05).

Conclusions Baricitinib plus TCS vs. placebo plus TCS showed significant improvements in treatment benefit at Week 16 and rapid significant improvements in HRQoL and impact of AD symptoms on work productivity and functioning through 16 weeks.

Received: 11 December 2020; Accepted: 17 March 2021

Conflicts of interest

AW has received grants, personal fees or non-financial support from AbbVie, Almirall, Beiersdorf, Biderma, Chugai, Eli Lilly and Company, Galapagos, Galderma, Hans Karrer, Leo Pharma, L’Oreal, Maruho, Medimmune, Novartis, Pfizer, Pierre Fabre, Regeneron, Santen and Sanofi-Aventis; TN has received speaker’s fees from Maruho and Sanofi; CM is an Investigator, Consultant, Advisory Board Member, Speaker for and/or receives honoraria from Aquinox Pharma, Asana BioSciences, AbbVie, Brickell Biotech, Dermavant, Eli Lilly and Company, Galderma, Glenmark, GSK-Steifel, Hoffman-LaRoche Ltd, Hoffman-LaRoche-Posay, Leo Pharma, Pfizer, Regeneron-Sanofi, Valeant and Vita; KP reports personal
fees from Almirall, AbbVie, Biogen, Janssen, Eli Lilly and Company, Celgene, Galderma, Janssen, Leo Pharma, Novartis, Pierre Fabre, Sanofi, Sandoz and Sun Pharma outside the submitted work; PL has served as an investigator for Abbvie and Regeneron/Sanofi-Genzyme, has served as an advisor/consultant for Abbvie, Arbonne, Amyris, Bodewell, Burt’s Bees, Dermavant, Derma, Eli Lilly and Company, Galderma, Johnson and Johnson, Kiniksa, Leo Pharma, L’Oreal, Micreos, Pfizer, Pierre Fabre, Regeneron/Sanofi-Genzyme, Theraplex and Verrica; has served as a speaker for Galderma, L’Oreal and Pfizer, and has a patent with Theraplex AIM. MA has served as advisor and/or paid speaker for and/or participated in research projects sponsored by Abbott/AbbVie, ALK Scherex, Almirall, Amgen, Beiersdorf, Biogen Idec, BMS, Boehringer Ingelheim, Celgene, Centocor, Dermira, Eli Lilly and Company, Forward Pharma, Fresenius, Galderma, GSK, Hexal, Incyte, Janssen-Cilag, LEO Pharma, Medac, Menlo, Merck, MSD, Mylon, Novartis, Pfizer, Regeneron, Sandoz, Sanofi-Aventis, Stallergenes, Stiefel, Teva, TK, Trevei, UCB and Xenopore; JJS has received honoraria as a consultant and/or advisory board member for Abbvie, Afyx, Arena, Asana, BioMX, Bluefin, Bodewell, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, Leo, Luna, Menlo, Novartis, Pfizer, RAPT, Regeneron, Sanofi; speaker for Pfizer, Regeneron, Sanofi; institution received grants from Galderma; MT has been a co-investigator for AbbVie, Boehringer, Eli Lilly and Company, Galderma, Janssen-Cilag, Leo Pharma, Pierre Fabre, Sanofi-Regeneron, and UCB and a speaker for Sanofi-Regeneron and Janssen-Cilag; CP has been an investigator and consultant for AbbVie, Almirall, Amgen, Boehringer, Celgene, Eli Lilly and Company, Galderma, Janssen-Cilag, Leo Pharma, Merck, Novartis, Pfizer, Pierre Fabre, Regeneron, Sanofi (AD) and UCB pharma; MJR, AMD, EP, FEY, LS and SB are employees and shareholders of Eli Lilly and Company.

Funding sources

Baricitinib is developed by Eli Lilly and Company, under licence from Incyte Corporation. The studies were funded by Eli Lilly and Company. All costs associated with the development of this manuscript including article processing charges and medical writing services, provided by Lydia Morris, PhD, of Syneos Health (Raleigh, NC), were funded by Eli Lilly and Company.

Introduction

Atopic dermatitis (AD) is a common, chronic, relapsing, highly symptomatic inflammatory skin disease. Pruritus is the primary source of morbidity in AD, and scratching can lead to bleeding and secondary infections associated with AD skin lesions. Worsening of pruritus at night can result in sleep disturbances. In addition to pruritus, patients report skin pain as an important symptom. The signs and symptoms of AD can have profound negative effects on patients’ health-related quality of life (HRQoL), including impaired work productivity and non-work activities, mental health and other HRQoL.

Current guidelines indicate emollients and topical corticosteroids (TCS) are the mainstay of AD treatment, where less severe AD can be controlled by appropriate skincare and TCS, but more severe AD usually requires additional treatments such as systemic medications or phototherapy. While systemic therapies can be effective, the risks for adverse events preclude their continuous long-term use, indicating the need for alternative treatments. Furthermore, despite the use of systemic therapies, most patients will still experience flares as part of their underlying disease. Thus, TCS are typically used intermittently as background therapy in combination with systemic medications to manage acute AD lesions. Dupilumab, a new injectable biologic, has been approved for the treatment of AD, showing short-term efficacy, long-term efficacy up to 76 weeks and a favourable benefit–risk profile in patients with AD. Despite this new advanced treatment, additional options are needed to fulfil patients’ unmet medical needs.

Baricitinib is an oral, selective and reversible Janus kinase 1 and 2 inhibitor approved in the European Union and Japan and under investigation in the United States and other countries for the treatment of moderate-to-severe AD in adult patients who are candidates for systemic therapy. Baricitinib is also approved in adults with moderately-to-severely active rheumatoid arthritis in 70 countries and is in late-stage development for adults with alopecia areata. In previous Phase 3 trials in adults with moderate-to-severe AD, once-daily oral baricitinib 4- and 2-mg were shown to be effective as monotherapy in treating patients with an inadequate response to TCS. Patients receiving baricitinib showed significant improvements in achieving clear or almost clear skin at 16 weeks vs. placebo. In a recent Phase 3 trial (BREEZE-AD7), baricitinib 4- and 2-mg therapy plus TCS were reported as effective in significantly improving the signs and symptoms of AD vs. placebo plus TCS in adults with moderate-to-severe AD with a previous inadequate response to TCS.

A patient’s perspective on their treatment is important in medical decision-making. Patient-reported outcome measures...
provide insights into how benefits in controlling symptoms extend to improvements in both disease severity and how AD affects functioning in work and daily life. From the BREEZE-AD7 study, we present efficacy of baricitinib plus TCS using functional measures of HRQoL, work productivity and life activities, symptom impact and treatment benefit in adults with moderate-to-severe AD with previous inadequate response to TCS.

Materials and methods

Study patients
Patients aged ≥18 years with a diagnosis of AD, as defined by the American Academy of Dermatology, at least 12 months before screening, were included. Eligible patients had a documented history of inadequate response to topical medications and thus met criteria for systemic therapy. Additional details on BREEZE-AD7 study design and patients, including settings and location where data were collected, blinding, randomisation and inclusion/exclusion criteria, are presented elsewhere.20

Compliance with ethics guidelines
The ethics review boards at each study site provided study protocol approval and informed consent form. The sponsor and investigators conducted the studies in accordance with the Declaration of Helsinki, applicable ICH-GCP guidelines, and applicable laws and regulations. Informed consent was obtained from all individual participants included in the studies or their legally acceptable representatives before study procedures were performed.

Study design
BREEZE-AD7 (NCT03733301) was a multicentre, randomised, double-blinded, placebo-controlled Phase 3 clinical trial. Patients were randomised 1 : 1 : 1 to receive oral placebo, baricitinib 2- or 4-mg plus TCS once daily for 16 weeks (Fig. S1). At baseline, patients were instructed to apply moderate potency TCS until lesions were clear or almost clear and then to switch to mild potency TCS for 7 days and then stop. If lesions reappeared, patients could resume the regimen. Patients experiencing unacceptable or worsening symptoms after 2 weeks of treatment may have been rescued with high- or ultra-high potency TCS or oral systemic agents. Patients who required rescue using oral systemic agents discontinued study treatment.

Patient-reported outcome measures and endpoints
The study objective was to evaluate the impact of baricitinib plus background TCS on patient-reported measures of HRQoL, AD symptom impact, work and daily life functioning, and treatment benefit.

The Dermatology Life Quality Index (DLQI) is a validated questionnaire covering various aspects of a patient’s HRQoL.21 Higher scores indicate greater impairment of HRQoL. A ≥4-point change from baseline in DLQI total score is considered the minimal clinically important difference;22 a total score from 2 to 5 indicates having a small effect on a patient’s HRQoL; and a total score of 0 to 1 indicates having no effect on a patient’s HRQoL.23

The Work Productivity and Activity Impairment-AD (WPAI-AD) questionnaire records impairment due to AD during the past 7 days.24 The WPAI-AD consists of four domains: absenteeism, presenteeism, work productivity loss (absenteeism plus presenteeism) and activity outside of work. Only employed patients answered questions related to absenteeism, presenteeism and work productivity loss; all patients answered the question related to activity outside of work. Scores are calculated as impairment percentages, with higher scores indicating greater impairment and less productivity.

Patient-Reported Outcome Measurement Information System (PROMIS) item banks are a set of person-centred measures that evaluate physical, mental and social health in adults and children.25,26 The PROMIS Itch Short Form instruments measure how much itch interferes with HRQoL in the past 7 days across several item banks.27–29 Patients also completed the PROMIS Sleep-Related Impairment Short Form instrument, which measures self-reported perceptions of impairment related to general aspects of sleep ‘in the past 7 days’.30–32 PROMIS instrument scores are T scores, where a higher score indicates greater impairment.

The Patient Benefit Index (PBI) measures patient-defined treatment objectives and benefits.33,34 A patient needs questionnaire is completed before treatment begins. Patients rate the importance of specific treatment goals from 0 ‘not important at all’ to 4 ‘very important’. During or at the end of treatment, the patient completes the Patient Benefit Questionnaire, in which the items are rated from 0 ‘did not help at all’ to 4 ‘helped a lot’. The PBI derives a global score for each patient from ratings on each questionnaire, with higher scores indicating greater benefit. Responses can also be scored based on 6 rating subscales scales: social impairment, psychological impairment, impairment due to therapy, physical impairment and confidence in therapy. Patients with PBI of 1 or greater are considered as having at least minimum patient-relevant treatment benefit.

Translations for the PROMIS instruments and PBI questionnaires were not available in all countries; thus, they were completed by a subset of the patients for whom translations were available according to language.

Statistical analysis
The analysis population comprised all randomised patients, regardless of whether they received the correct treatment. Treatment comparisons between baricitinib and placebo for DLQI categorical endpoints [≥4-point improvement in DLQI total
score, DLQI total score ≤5 and DLQI (0,1)] were performed using logistic regression analysis with region, baseline vIGA-AD, baseline value and treatment group as factors. Only patients with baseline DLQI total score ≥4 for the 4-point or more improvement endpoint and patients with baseline DLQI total score >5 for the DLQI total score ≤5 endpoint were included. Mean change from baseline for continuous measures (PROMIS and WPAI-AD) was evaluated using a restricted maximum likelihood-based mixed model repeated measures (MMRM), where the model includes treatment, region, baseline disease severity [validated Investigator Global Assessment for AD (vIGA-AD)], visit and treatment-by-visit-interactions as fixed categorical effects and baseline and baseline-by-visit-interaction as fixed continuous effects. Treatment comparisons for PBI scores were analysed using an analysis of variance model, where treatment, region and baseline vIGA-AD were included as factors. The P-values for treatment comparisons were not adjusted for multiplicity.

Data collected after first rescue therapy or permanent study drug discontinuation were considered missing. Non-responder imputation was used to impute missing values for categorical variables. No explicit imputations were conducted for continuous measures; MMRM analysis was performed to mitigate the impact of missing data because it yields valid inferences assuming that missing observations are missing-at-random. Observed data were used to analyse continuous PBI scores as the postbaseline data were collected only once during the treatment period. Per the study protocol, WPAI-AD outcomes were prespecified as secondary objectives, and DLQI, PROMIS and PBI outcomes were prespecified as exploratory objectives. Statistical analyses were performed using SAS® version 9.4 or higher (SAS Institute, Cary, NC, USA).

Results

Subject disposition and demographics

Patient demographic and baseline characteristics are presented in Table 1. As reported previously, 329 patients were randomised in the study (placebo + TCS, N = 109; baricitinib 4-mg + TCS, N = 111; baricitinib 2-mg + TCS, N = 109). Baseline characteristics and illness severity measures were similar across treatment groups. High impairment of HRQoL at baseline was indicated by a mean DLQI total score of 15.2. Study discontinuation included 6.4% in the placebo plus TCS group, 3.6% in the baricitinib 4-mg plus TCS group and 8.3% in the baricitinib 2-mg plus TCS group. The rate of rescue therapy was 9.2% in the placebo group, 4.6% in baricitinib 2-mg and 5.4% in the baricitinib 4-mg group.

Table 1 Demographics and baseline characteristics of patients

| Parameter                  | PBO + TCS |
|----------------------------|-----------|
| Age, years                 | 33.7 (13.2) |
| Female, %                  | 34.9      |
| Race, %                    |           |
| Caucasian                  | 42.2      |
| Asian                      | 52.3      |
| Multiple                   | 5.5       |
| Prior systemic therapy use, % | 68.8    |
| Prior cyclosporine use, %  | 37.9      |
| BSA affected by AD         | 48.1 (24.4) |
| vIGA-AD of 4 at baseline, %| 44.4      |
| Itch NRS                   | 7.4 (1.7)  |
| DLQI                       | 15.0 (7.9) |
| WPAI-AD                    |           |
| Activity                   | 52.9 (28.0) |
| Presenteeism               | 43.0 (26.5) |
| Absenteeism                | 10.9 (25.5) |
| Work productivity loss     | 45.8 (28.5) |
| PROMIS Itch                |           |
| Scratching behaviour       | 59.8 (7.5)  |
| Interference               | 53.7 (8.8)  |
| Mood and sleep             | 58.9 (8.6)  |
| Activity and clothing      | 56.4 (9.3)  |
| Sleep-related impairment   | 60.6 (10.7) |
**DLQI**

At Week 2, significantly greater proportions of patients in both baricitinib plus TCS treatment groups vs. placebo plus TCS reported scores that met or exceeded the minimal clinically important difference threshold for DLQI total score (≥4-point improvement; Fig. 1a). Similarly, significantly greater proportions of patients in baricitinib plus TCS treatment groups vs. placebo plus TCS reported scores indicating AD symptoms had no more than a small effect on patient HRQoL (DLQI total score ≤5) or had no effect [DLQI (0,1)] starting at Week 2 (baricitinib 4-mg plus TCS) or Week 4 (baricitinib 2-mg plus TCS; Fig. 1b, c). Overall, statistically significant improvements in HRQoL observed within the first 8 weeks were sustained through Week 16, except for DLQI total score ≥4-point improvement in the 2-mg baricitinib plus TCS group (Fig. 1a).

**WPAI-AD**

Patients treated with baricitinib 4- or 2-mg plus TCS demonstrated significantly less impairment in daily activities vs. patients treated with placebo (Fig. 2a). These differences

---

**Figure 1** Dermatology Life Quality Index Outcomes (NRI). Proportion of patients achieving (a) 4 or more point improvement in DLQI total score; (b) a DLQI total score ≤5; and (c) a 0 or 1 on the DLQI, in patients receiving BARI 4-, 2-mg and placebo plus TCS through Week 16. P-values for BARI vs. PBO: *P ≤ 0.05, **P ≤ 0.01, ***P ≤ 0.001, BARI, baricitinib; BL, baseline; DLQI, Dermatology Life Quality Index; NRI, non-responder imputation; Nx, number of patients with non-missing values; PBO, placebo; TCS, topical corticosteroids. Table beneath the graph includes number of patients with non-missing values at the indicated time points. Patient population includes all randomised patients. Patients from the analysis shown in panel (a) had a baseline DLQI total score ≥4 and panel (b) had a baseline DLQI total score ≥5. DLQI (0,1) categorical data were previously reported. © 2021 Eli Lilly and Company. Journal of the European Academy of Dermatology and Venereology published by John Wiley & Sons Ltd on behalf of European Academy of Dermatology and Venereology.
occurred at Week 1 and continued through Week 16. Similarly, patients treated with baricitinib 4-mg plus TCS vs. placebo plus TCS experienced significant reductions in presenteeism through Week 16 (Fig. 2b); there were no differences across treatments for absenteeism (Fig. 2c). Overall work productivity loss mirrored results for presenteeism (Fig. 2d).

PROMIS Itch

Scratching behaviour At Week 1, statistically significant improvements from baseline were observed in the baricitinib 4-mg plus TCS treatment group vs. placebo plus TCS for the scratching behaviour outcome, and improvements were sustained through Week 16 (Fig 3a). Statistically significant improvements from baseline were also observed in the baricitinib 2-mg plus TCS treatment group vs. placebo plus TCS at Week 2.

Itch interference At Week 2, statistically significant improvements from baseline were observed in the baricitinib 4-mg plus TCS treatment group vs. placebo plus TCS for the itch interference outcome, and improvements were sustained through Week 16 (Fig. 3b). A statistically significant improvement from baseline was also observed in the baricitinib 2-mg plus TCS treatment group vs. placebo plus TCS at Week 16.

Mood and sleep At Week 1, statistically significant improvements from baseline were observed in the baricitinib 4-mg plus
Figure 3 Patient-Reported Outcome Measurement Information System Item Banks (MMRM). Change from baseline in PROMIS Itch item banks (a) scratching behaviour, (b) interference, (c) mood and sleep, (d) activity and clothing items, and (e) sleep-related impairment in patients receiving BARI 4-, 2-mg and PBO plus TCS through Week 16. P-values for BARI vs. PBO: *P ≤ 0.05, **P ≤ 0.01, ***P ≤ 0.001. BARI, baricitinib; BL, baseline; MMRM, mixed effect repeated measure; Nx, number of patients with non-missing values; PBO, placebo; PROMIS, Patient-Reported Outcome Measurement Information System; TCS, topical corticosteroids. Table beneath the graph includes number of patients with non-missing values at the indicated time points. Table beneath the graph includes number of patients with non-missing values at the indicated time points. A subset of patients for whom translations were available according to language completed the PROMIS instruments. Patient population includes all randomised patients. PROMIS instrument scores are T scores, where a higher score indicates greater impairment.
TCS treatment group vs. placebo plus TCS for the mood and sleep outcome, and improvements were sustained through Week 16 (Fig. 3c). A statistically significant improvement from baseline was also observed in the baricitinib 2-mg plus TCS treatment group vs. placebo plus TCS at Week 4.

Activity and clothing At Week 1, statistically significant improvements from baseline were observed in the baricitinib 4-mg plus TCS treatment group vs. placebo plus TCS for the activity and clothing outcome (Fig. 3d). Improvements were sustained through Week 16 (Fig. 3d).

PROMIS sleep-related impairment Patients treated with baricitinib 4-mg plus TCS reported significantly greater improvement in daytime sleep functioning related to sleep loss at Week 4 vs. patients treated with placebo plus TCS, and this improvement was sustained through Week 16 (Fig. 3e).

PBI At Week 16, patients treated with either baricitinib 4-mg plus TCS or 2-mg plus TCS had a significantly greater PBI total score vs. patients treated with placebo plus TCS (Fig. 4a). For the PBI subscales, patients who received baricitinib 4 mg plus TCS had significantly greater goal attainment related to social impairment, psychological impairment, impairment due to therapy, physical impairment and confidence in healing than patients treated with placebo plus TCS. Patients who received baricitinib 2-mg plus TCS had similar results for the goals related to psychological impairment, impairment due to therapy and confidence in healing. Significantly greater proportions of patients in both baricitinib plus TCS treatment groups vs. placebo plus TCS reported a PBI total score that met or exceeded the minimum patient-relevant treatment benefit (Fig. 4b).

Discussion Moderate-to-severe AD can have a profound negative effect on HRQoL, reflected by high mean DLQI values observed at baseline in this study. Results reported here demonstrated that baricitinib 2- and 4-mg plus TCS result in improved HRQoL, work productivity, daily life functioning and symptom impact.

A greater proportion of patients treated with baricitinib 2- or 4-mg plus TCS achieved statistically significant improvements vs. patients treated with placebo plus TCS in ≥4-point improvement in DLQI total score (baricitinib 4-mg plus TCS only), DLQI total score ≤5 endpoint and DLQI (0,1). Approximately 60% and 40% of patients with baricitinib 4- and 2-mg plus TCS, respectively, reported AD symptoms had a small impact on their life (DLQI total score ≤5) through Week 16.

Pruritus is the main morbidity affecting patients with AD and contributes to other conditions including sleeplessness and anxiety/depression. Baricitinib 4-mg plus TCS improved HRQoL related to pruritus and sleeplessness, as shown by mean improvements in the PROMIS instruments. PROMIS results
also revealed decreased scratching behaviour due to pruritus and decreased interference in life choices, including selection of activities and clothing. Thus, while baricitinib was previously shown to relieve the severity of itch, often within 1 or 2 days of beginning therapy, these findings reinforce that symptom relief translates to improved functioning in work and daily life beginning soon after the start of therapy.

In addition to improvements in HRQoL and symptom impact, this study also demonstrates that treatment with baricitinib plus TCS increases work productivity. Presenteeism refers to the outcome in which patients may be physically present at work, but their ability to work efficiently and remain focused is compromised. Given the nature of pruritus, impact on work functioning is typically observed by greater presenteeism than absenteeism because the continual presence of pruritus impairs concentration. Findings reported here are consistent with these observations in that, while absenteeism was not problematic, patients had a significant percentage of time at work captured as presenteeism, which then showed early and sustained improvement with baricitinib plus TCS therapy. Consistent with the DLQI outcomes, patients, including non-employed patients, also found that baricitinib therapy plus TCS improved their engagement in non-work activities.

Baricitinib previously demonstrated efficacy in treating AD as a monotherapy and plus TCS. The use of TCS in this study mirrors clinical practice where TCS is a supplement for treatment of active lesions. Patients’ goals are a necessary component of treatment decision-making. In this study, patients’ goals were assessed using the PBI, and the majority of patients treated with baricitinib indicated benefits in achieving relevant personal goals previously defined by the individual patient. The benefits included both satisfaction with improvements in emotional and physical goals as well as confidence in treatment and satisfaction with overall treatment burden, showing a significant added value with use of baricitinib plus TCS therapy.

A limitation of these studies is that generalizability of these findings might be limited by the demographics of the study populations, over-representing relatively young adult white men. Another limitation is that the PROMIS and PBI measures were only available for a subset of the patients. However, given that the baseline demographics and characteristics were similar across treatment groups, this limitation does not appear to have introduced bias for these measures. The WPAI-AD, PROMIS and PBI measures are not yet employed to assess patient outcomes in a clinical form may be too lengthy for routine clinical use; however, each measure was validated for feasibility and reliability in clinical studies and should provide information about if and to what extent patient-defined objectives and benefits were met. Another consideration is that AD is a chronic disease that often follows a relapsing–remitting cycle over a patients’ lifetime; thus, the 16-week timeframe should be expanded to completely understand the effects of baricitinib treatment on patient-reported outcomes and the durability of these results. Additional studies of baricitinib as a long-term therapy in AD are underway and will provide evidence of the longer persistence of these treatment benefits.

In summary, daily treatment with baricitinib 2- and 4-mg plus TCS, vs. placebo plus TCS, achieved clinically meaningful results in patient-reported outcomes. While improving severity of skin disease remains the primary focus to evaluate treatment efficacy, incorporating the patient perspective and assessing functional impacts of treatment remain integral to evaluating the overall treatment benefit. Here, baricitinib 2- and 4-mg plus TCS therapy resulted in early benefits in HRQoL, symptom impact and patient function across life domains that were sustained to Week 16 and resulted in overall treatment benefit.

**Acknowledgements**

The patients in this manuscript have given written informed consent to publication of their case details. We would like to thank the patients who participated in the study and all investigators and study personnel who enrolled, collected data and cared for the patients. We thank Margaret Gamalo, PhD, for statistical input.

**References**

1. Bylund S, von Kobyletzki LB, Svalstedt M, Svensson Å. Prevalence and incidence of atopic dermatitis: a systematic review. Acta Derm Venereol 2020; 100: adv00160.
2. American Academy of Dermatology Association. Eczema Types: Atopic Dermatitis Symptoms, 2020. URL https://www.aad.org/public/diseases/eczema/types/atopic-dermatitis/symptoms (last accessed: 24 September 2020).
3. Abuabara K, Yu AM, Okhovat J-P, Allen IE, Langan SM. The prevalence of atopic dermatitis beyond childhood: a systematic review and meta-analysis of longitudinal studies. Allergy 2018; 73: 696–704.
4. Weidinger S, Beck LA, Bieber T, Kabashima K, Irvine AD. Atopic dermatitis. Nature Reviews Disease Primers 2018; 4: 1.
5. Simpson EL. Comorbidity in atopic dermatitis. Current Dermatol Rep 2012; 1: 29–38.
6. Silverberg JI, Gelfand JM, Margolis DJ et al. Patient burden and quality of life in atopic dermatitis in US adults: a population-based cross-sectional study. Ann Allergy Asthma Immunol 2018; 121: 340–347.
7. Avena-Woods C. Overview of atopic dermatitis. Am J Manag Care 2017; 23: S115–S123.
8. Langenbruch A, Radtke M, Franzeke N, Ring J, Foelster-Holth R, Augustin M. Quality of health care of atopic eczema in Germany: results of the national health care study AtopicHealth. J Eur Acad Dermatol Venereol 2014; 28: 719–726.
9. Yano C, Saeki H, Ishiji T et al. Impact of disease severity on sleep quality in Japanese patients with atopic dermatitis. J Dermatol Sci 2013; 72: 195–197.
10. Vakharia PP, Chopra R, Sacotte R et al. Burden of skin pain in atopic dermatitis. Ann Allergy Asthma Immunol 2017; 119: 548–552.e543.
11. Thyssen JP, Hamann CR, Linneberg A et al. Atopic dermatitis is associated with anxiety, depression, and suicidal ideation, but not with psychiatric hospitalization or suicide. Allergy 2018; 73: 214–220.
12. Eckert L, Gupta S, Amund C, Gadkari A, Mahajan P, Gelfand JM. Impact of atopic dermatitis on health-related quality of life and productivity in...
adults in the United States: an analysis using the National Health and Wellness Survey. J Am Acad Dermatol 2017; 77: 274–279.e273.
13 Eckert L, Gupta S, Gadkari A, Mahajan P, Gelfand JM. Burden of illness in adults with atopic dermatitis: analysis of National Health and Wellness Survey data from Germany, Italy, Spain, and the United Kingdom. J Am Acad Dermatol 2019; 81: 187–195.
14 Holm JG, Agner T, Clausen ML, Thomsen SF. Quality of life and disease severity in patients with atopic dermatitis. J Eur Acad Dermatol Venereol 2016; 30: 1760–1767.
15 Deleuran M, Thac D, Beck LA et al. Dupilumab shows long-term safety and efficacy in patients with moderate to severe atopic dermatitis enrolled in a phase 3 open-label extension study. J Am Acad Dermatol 2020; 82: 377–388.
16 Thac D, L. Simpson E, Deleuran M, et al. Efficacy and safety of dupilumab monotherapy in adults with moderate-to-severe atopic dermatitis: a pooled analysis of two phase 3 J Dermatol Sci 2019; 94: 266–275. randomized trials (LIBERTY AD SOLO 1 and LIBERTY AD SOLO 2).
17 Fridman JS, Scherle PA, Collins R et al. Selective inhibition of JAK1 and JAK2 is efficacious in rodent models of arthritis: preclinical characterization of INCB028050. J Immunol 2010; 184: 5298–5307.
18 www.ema.europa.eu. 2020. Olumiant 2mg and 4mg film-coated tablets - Summary of Product Characteristics (SPC) - (eMC). [online] URL https://www.ema.europa.eu/en/medicines/human/EPAR/olumiant#prod uct-information-section (last accessed: 24 May 2021).
19 Simpson EL, Lacour JP, Spelman L 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. Br J Dermatol 2020; 183: 242–255.
20 Reich K, Kabashima K, Peris K et al. Efficacy and safety of baricitinib combined with topical corticosteroids for treatment of moderate to severe atopic dermatitis: a randomized clinical trial. JAMA Dermatol 2020; 156: 1333.
21 Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)—a simple practical measure for routine clinical use. Clin Exp Dermatol 1994; 19: 210–216.
22 Basra MK, Salek MS, Camilleri L, Sturkey R, Finlay AY. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. Dermatology 2015; 230: 27–33.
23 Hongbo Y, Thomas CL, Harrison MA, Salek MS, Finlay AY. Translating the science of quality of life into practice: what does dermatology life quality index scores mean? J Invest Dermatol 2005; 125: 659–664.
24 Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmaco eco-nomics 1993; 4: 353–365.
25 Silverberg JJ, Kantor RW, Dalal P et al. A comprehensive conceptual model of the experience of chronic itch in adults. Am J Clin Dermatol 2018; 19: 759–769.
26 Health Measures. PROMIS, 2019. URL http://www.healthmeasures.net/ explore-measurement-systems/promis (last accessed: 18 June 2020).
27 Health Measures. ITCH A Brief Guide to the PROMIS® Itch Instruments, 2020. URL http://www.healthmeasures.net/images/PROMIS/manuals/PROMIS_ITCH_Scoring_Manual.pdf (last accessed: 9 March 2020).
28 Silverberg JJ, Lai JS, Kantor RW et al. Development, validation, and interpretation of the PROMIS itch questionnaire: a patient-reported outcome measure for the quality of life impact of itch. J Invest Dermatol 2020; 140: 986–994.e986.
29 Silverberg JJ, Lai JS, Vakharia PP et al. Measurement properties of the patient-reported outcomes measurement information system itch questionnaire item banks in adults with atopic dermatitis. J Am Acad Dermatol 2020; 82: 1174–1180.
30 Health Measures. SLEEP-RELATED IMPAIRMENT A brief guide to the PROMIS® Sleep-Related Impairment instruments, 2020. URL https:// www.healthmeasures.net/images/PROMIS/manuals/PROMIS_Sleep-Relat ed_Impairment_Scoring_Manual.pdf (last accessed: 14 April 2020).
31 Buyssse DJ, Yu L, Moul DE et al. Development and validation of patient-reported outcome measures for sleep disturbance and sleep-related impairments. Sleep 2010; 33: 781–792.
32 Lei DK, Yousa M, Janmohamed SB et al. Validation of patient-reported outcomes information system sleep disturbance and sleep-related impairment in adults with atopic dermatitis. Br J Dermatol 2020; 183: 875–882.
33 Augustin M, Radtke MA, Zschocke I et al. The patient benefit index: a novel approach in patient-defined outcomes measurement for skin diseases. Arch Dermatol Res 2009; 301: 561–571.
34 Blome C, Augustin M, Behechtnejad J, Rustenbach SJ. Dimensions of patient needs in dermatology: subscales of the patient benefit index. Arch Dermatol Res 2011; 303: 11–17.
35 Oh SH, Bae BG, Park CO et al. Association of stress with symptoms of atopic dermatitis. Acta Derm Venereol 2010; 90: 582–588.
36 Chrostowska-Plak D, Reich A, Szpiewtowski JC. Relationship between itch and psychological status of patients with atopic dermatitis. J Eur Acad Dermatol Venereol 2013; 27: e239–e242.
37 Simpson EL, Lacour JP, Spelman L 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. Br J Dermatol 2020; 183: 242–255.
38 Chung J, Simpson EL. The socioeconomic of atopic dermatitis. Ann Allergy Asthma Immunol 2019; 122: 360–366.

Supporting information
Additional Supporting Information may be found in the online version of this article:
Figure S1. Study design.