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Impact of Ruxolitinib Cream on Work Productivity and Activity Impairment and Associated Indirect Costs in Patients with Atopic Dermatitis: Pooled Results From Two Phase III Studies

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Abstract

Background Atopic dermatitis is a chronic inflammatory skin disease that can negatively impact work productivity and daily activities. Ruxolitinib cream, a Janus kinase inhibitor, demonstrated efficacy and safety in patients with atopic dermatitis in two phase III studies (TRuE-AD1 and TRuE-AD2).

Objective This post hoc analysis sought to describe the effects of ruxolitinib cream on work productivity and activity impairment from pooled data from the phase III studies, to estimate indirect costs due to atopic dermatitis, and to estimate the incremental cost savings with ruxolitinib cream versus vehicle cream.

Methods Patients in both studies were ≥ 12 years old with atopic dermatitis for ≥ 2 years, an Investigator's Global Assessment score of 2 or 3, and a 3–20% affected body surface area at baseline. Patients were randomized 2:2:1 to receive ruxolitinib cream (0.75% or 1.5%) or vehicle cream for 8 weeks. Patient self-reported productivity in the efficacy-evaluable population was assessed at weeks 2, 4, and 8 using the Work Productivity and Activity Impairment Questionnaire-Specific Health Problem version 2.0. Statistical significance for the two doses versus vehicle was calculated using an analysis of covariance. Work Productivity and Activity Impairment overall work impairment scores were converted to a model of costs per employed patient due to lost productivity and incremental cost savings from ruxolitinib cream treatment using a human capital approach.

Results Of 1249 patients enrolled (median age, 32 years; female sex, 61.7%), 1208 were included in the efficacy-evaluable population. Patients applying 0.75% or 1.5% ruxolitinib cream had significant changes in overall work impairment ($-17.9%$ [0.75% strength] and $-15.0%$ [1.5% strength] vs $-5.7%$ for vehicle; $p < 0.0001$ for both) and daily activity impairment ($-20.6%$ [0.75% strength] and $-21.5%$ [1.5% strength] vs $-10.6%$ for vehicle; $p < 0.0001$ for both). These corresponded to estimated lost productivity costs in 2021 US dollars of \$1313 (0.75% strength) and \$1242 (1.5% strength) versus \$2008 (vehicle) over the 8-week trial period. Compared with a patient receiving vehicle, incremental annual indirect cost savings were estimated to be \$5302 with 0.75% ruxolitinib cream and \$4228 with 1.5% ruxolitinib cream.

Conclusions Ruxolitinib cream therapy is associated with improved work productivity and daily activity compared with vehicle and is estimated to reduce the indirect cost burden on the patient.

Clinical trial registration ClinicalTrials.gov identifiers: NCT03745638 (registered 19 November, 2018) and NCT03745651 (registered 19 November, 2018)

Key Points

Treatment of atopic dermatitis with ruxolitinib cream significantly improved patient-reported measures of work productivity and daily activity impairment.

Using a human capital approach, incremental annual indirect cost savings for patients applying 0.75% or 1.5% ruxolitinib cream were estimated to be \$5302 and \$4228, respectively.

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1 Background

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by itching, dryness, and redness that occurs in approximately 10–15% of children and 5–10% of adults in the USA [1–4]. Atopic dermatitis is associated with pruritus, skin pain, frequent flares, depression, anxiety, and sleep deprivation that can negatively impact work productivity and daily activities [2, 5, 6]. Even patients with mild AD and their caregivers may incur substantial indirect costs based on missed days or lost productivity at work and career modification and have reduced quality of life [7].

Janus kinases (JAKs) play important roles in the pathogenesis of AD and itch by mediating proinflammatory cytokines in skin and sensory neurons [8, 9]. A topical cream formulation of ruxolitinib, a selective inhibitor of JAK1 and JAK2 [10], is approved by the US Food and Drug Administration for the treatment of patients with mild to moderate AD aged at least 12 years who are not immunocompromised and whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable [11]. Regulatory approval was based on two phase III AD studies of identical design (Topical Ruxolitinib Evaluation in Atopic Dermatitis [TRuE-AD] 1 [NCT03745638] and TRuE-AD2 [NCT03745651]), in which ruxolitinib cream demonstrated anti-inflammatory activity with antipruritic action versus vehicle and was well tolerated [12]. The objective of this post hoc analysis was to describe the effects of ruxolitinib cream on work productivity and activity impairment based on pooled data from these two phase III trials in adolescent and adult patients with AD. From these data, the overall associated indirect costs from lost productivity to the individual patient were estimated.

2 Methods

2.1 Patients and Study Design

The two phase III studies of identical design, TRuE-AD1 (NCT03745638) and TRuE-AD2 (NCT03745651), were randomized, double-blind, and vehicle controlled, and the results were previously reported [12]. Eligible patients were aged at least 12 years with AD for at least 2 years and had an Investigator's Global Assessment (IGA) score of 2 or 3 and an affected body surface area of 3–20% (excluding scalp). Patients were randomized 2:2:1 to one of two ruxolitinib cream strength regimens (0.75% or 1.5%) or vehicle cream, applied twice daily as continuous treatment of initially affected areas over an 8-week double-blind trial period. Additional details regarding patients and study design were previously reported [12].

2.2 Assessments

In both studies, patient self-reported productivity was assessed using the Work Productivity and Activity Impairment Questionnaire-Specific Health Problem version 2.0 (WPAI:SHP v2.0) at weeks 2, 4, and 8. The WPAI:SHP v2.0 is a six-item questionnaire that measures the effect of overall health and specific symptoms on productivity at work and regular activity outside of work during the previous 7 days, including work time missed due to AD (absenteeism), impairment while working with AD (presenteeism), overall AD-related work impairment (absenteeism and presenteeism), and AD-related activity impairment. Scores are expressed as a percentage of impairment, with higher scores indicating greater impairment [13]. Only patients who self-identified as having paid employment were asked questions regarding absenteeism, presenteeism, and overall work impairment.

2.3 Statistical Analysis

All analyses were conducted in the efficacy-evaluable population using the pooled data from both studies. The statistical significance of changes from baseline in WPAI:SHP scores at weeks 2, 4, and 8 was assessed using an analysis of covariance.

2.4 Indirect Cost Model

The WPAI overall work impairment scores were used to assess the cost of lost productivity and potential cost savings per employed patient resulting from the use of ruxolitinib cream using a human capital approach. Scores at week 6 were imputed as the means of weeks 4 and 8. The proportion of time with impairment was combined with epidemiologic data on employment status among patients with AD (full time, 79%; part time, 21%) [5] and the median weekly wage from the 2021 US Bureau of Labor Statistics (Table 1) [14]. Employees were stratified by full-time versus part-time employment based on a published study of employment status in patients with AD [5]. Age-specific and sex-specific median weekly wages for full-time and part-time workers were extracted from Bureau of Labor Statistics data and used to create a weighted average weekly wage in 2021 US dollars for patients with AD, considering baseline age and sex. This weighted average cost per week was multiplied by the proportion of overall work impairment, overall and by treatment arm. Indirect costs were calculated based on the baseline WPAI:SHP v2.0 scores

(untreated) and those from the vehicle-controlled period (treated). Variance in incremental indirect cost savings was calculated from the upper and lower bounds of the 95% confidence interval for the mean difference in overall work impairment at each timepoint.

3 Results

3.1 Patients

Overall, 1249 patients (median age, 32 years; female sex, 61.7%) were randomized in the two trials (vehicle, $n = 250$; 0.75% ruxolitinib cream, $n = 500$; 1.5% ruxolitinib cream, $n = 449$), and 1208 patients were included in the efficacy analysis [12]. Of these, 678 (56.1%) completed at least one of the work-related questions, and 1205 (99.8%) completed the daily activity impairment question of the WPAI:SHP. Distribution of baseline demographics and clinical characteristics was similar across treatment groups. Across cohorts in the efficacy-evaluable population, 68.6% were White, 24.2% were Black, 3.8% were Asian, and 3.4% were other races (Table 2). Most patients (74.2%) had a baseline IGA score of 3. Mean (standard deviation [SD]) itch numeric rating scale score was 5.1 (2.4) at baseline; 64.4% of patients had a score of at least 4.

3.2 WPAI Scores

Improvements in WPAI:SHP scores among patients randomized to ruxolitinib cream (0.75% or 1.5%) versus vehicle were observed at weeks 2, 4, and 8 for domains of presenteeism, overall work impairment, and daily activity impairment (Fig. 1 and Table 3). Statistically significant differences in percentage change from baseline versus vehicle at week 8

were observed for presenteeism (-19.2% / -19.8% for 0.75%/1.5% strength vs -12.3% for vehicle; $p < 0.0001$ for both), overall work impairment (-17.9% / -15.0% vs -5.7% ; $p < 0.0001$ for both), and daily activity impairment (-20.6% / -21.5% vs -10.6% ; $p < 0.0001$ for both). Significant differences at week 8 were noted for absenteeism with 0.75% ruxolitinib cream versus vehicle (1.3% vs 7.4%; $p < 0.05$), and 1.5% ruxolitinib cream (4.8%) showed a trend toward difference versus vehicle.

3.3 Indirect Costs

Estimated indirect costs per employed patient were lower for patients using either strength of ruxolitinib cream versus patients using vehicle (Table 4). These costs were lower for each 2-week period of the 8-week vehicle-controlled period. Total estimated indirect cost savings per patient over the 8-week trial period for 0.75% and 1.5% ruxolitinib cream versus vehicle were \$695 and \$766, respectively (Fig. 2A). Over a 1-year horizon, reductions in indirect costs owing to treatment were estimated to be \$2127 for vehicle cream, \$7428 for 0.75% ruxolitinib cream, and \$6355 for 1.5% ruxolitinib cream (Fig. 2B). Incremental indirect cost savings compared with patients randomized to vehicle cream were estimated to be \$5302 (\$5126–\$5477) and \$4228 (\$3987–\$4469) for patients randomized to 0.75% and 1.5% ruxolitinib cream, respectively.

4 Discussion

In pooled results from two phase III trials, patients with AD who had an IGA score of 2 or 3, an affected body surface area of 3–20%, and applied either 0.75% or 1.5% ruxolitinib cream reported improvement in work productivity versus vehicle, with significant improvements in presenteeism (19.2%/19.8% vs 12.3%), overall work impairment scores (17.9%/15.0% vs 5.7%), and activity impairment (20.6%/21.5% vs 10.6%) scores at week 8. Previous studies in patients with psoriasis [15] and psoriatic arthritis [16] suggest that a 15–20% improvement in each WPAI:SHP domain is clinically meaningful, defined as the minimal improvement in an outcome that is perceived by patients as being beneficial. Improvements in work productivity with ruxolitinib cream are generally comparable to results obtained in other studies with oral JAK inhibitors in patients with moderate to severe AD. Patients who were treated with abrocitinib, an oral JAK1 inhibitor, reported a 22.9% reduction in overall work impairment after 12 weeks of therapy compared with 5.0% for treatment with placebo [17]. The combination of topical corticosteroid cream with baricitinib, an oral JAK1/JAK2 inhibitor, in adult patients with AD eligible for systemic treatment reduced the

Table 1 Model inputs [5, 12, 14]

Characteristic (source for input)	Input
Demographic	
Median age, years [12]	32.0
Female, % [12]	61.7
Employment status, % [5]	
Full time	79
Part time	21
Median weekly wage, 2021 US\$ [14]	
Full time	
Male	968
Female	843
Part time	
Male	375
Female	356

Table 2 Patient demographics and baseline clinical characteristics in the efficacy-evaluable population

Characteristic	Vehicle (<i>n</i> = 244)	0.75% Ruxolitinib cream (<i>n</i> = 483)	1.5% Ruxolitinib cream (<i>n</i> = 481)	Total (<i>N</i> = 1208)
Age, median (range), years	34 (12–82)	34 (12–85)	31 (12–85)	32 (12–85)
Age category, <i>n</i> (%), years				
12–17	43 (17.6)	106 (21.9)	87 (18.1)	236 (19.5)
≥ 18	201 (82.4)	377 (78.1)	394 (81.9)	972 (80.5)
Female, <i>n</i> (%)	154 (63.1)	292 (60.5)	293 (60.9)	739 (61.2)
Race, <i>n</i> (%)				
White	164 (67.2)	328 (67.9)	337 (70.1)	829 (68.6)
Black	61 (25.0)	118 (24.4)	113 (23.5)	292 (24.2)
Asian	10 (4.1)	16 (3.3)	20 (4.2)	46 (3.8)
Other	9 (3.7)	21 (4.3)	11 (2.3)	41 (3.4)
Region, <i>n</i> (%)				
North America	172 (70.5)	342 (70.8)	341 (70.9)	855 (70.8)
Europe	72 (29.5)	141 (29.2)	140 (29.1)	353 (29.2)
BSA, mean (SD), %	9.5 (5.4)	9.7 (5.2)	9.4 (5.2)	9.6 (5.2)
Baseline EASI, mean (SD)	7.8 (4.8)	8.1 (4.9)	7.8 (4.8)	7.9 (4.9)
Baseline IGA, <i>n</i> (%)				
2	64 (26.2)	125 (25.9)	123 (25.6)	312 (25.8)
3	180 (73.8)	358 (74.1)	358 (74.4)	896 (74.2)
Itch NRS score, mean (SD)	5.2 (2.5)	5.1 (2.4)	5.1 (2.5)	5.1 (2.4)
≥ 4, <i>n</i> (%)	158 (64.8)	313 (64.8)	307 (63.8)	778 (64.4)
PROMIS sleep disturbance score, mean (SD)	18.7 (5.8)	19.1 (6.1)	19.0 (6.1)	18.9 (6.1)
PROMIS sleep-related impairment score, mean (SD)	16.8 (6.1)	17.3 (6.2)	17.4 (6.2)	17.2 (6.2)
Duration of disease, median (range), years	16.5 (0.8–79.1)	14.8 (0.1–68.8)	15.9 (0–69.2)	15.3 (0–79.1)
Number of flares in the past 12 months, mean (SD)	7.3 (26.0)	5.1 (6.7)	5.8 (17.9)	5.8 (16.8)

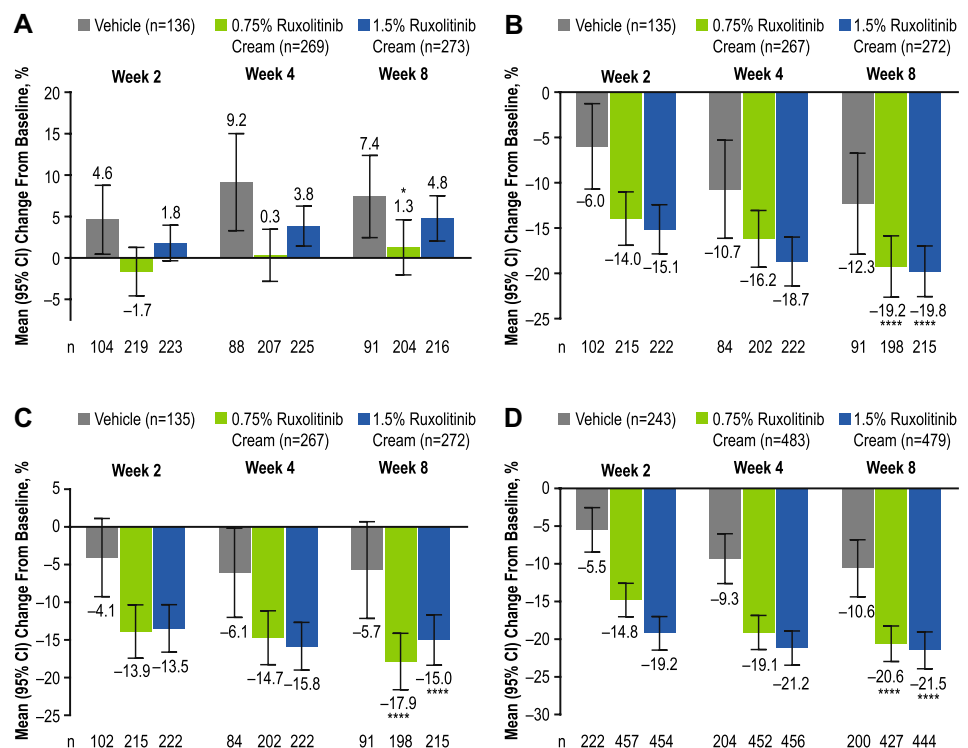
BSA body surface area, EASI Eczema Area and Severity Index, IGA Investigator's Global Assessment, NRS numeric rating scale, PROMIS Patient-Reported Outcomes Measurement Information System, SD standard deviation

overall work impairment by 26.3%, compared with 12.2% for topical corticosteroids and placebo, after 2 weeks of therapy [18]. Although no real-world observational data are available for other JAK inhibitors in AD, improvements in work productivity with the application of ruxolitinib cream also compared favorably with improvements with dupilumab observed in Dutch patients with moderate to severe AD (mean [SD] baseline impairment, 35.5% [28.5%]; mean [SD] impairment at 52 weeks, 11.5% [18.4%]) [19]. Of note, underlying comorbidities may have an impact on work productivity. For example, in the Dutch patients, the mean (SD) improvement from baseline in overall work impairment significantly differed between patients who did not have self-reported asthma (– 30.6% [29.4%]) and those who had self-reported asthma (– 19.9% [26.3%]) [19]. Furthermore, claims database analyses of patients in the USA found that nonresponse with systemic agents, such as conventional immunosuppressive agents or dupilumab, was significantly associated with having comorbid respiratory conditions [20] and that 59% of non-responders to dupilumab had Quan-Charlson Comorbidity Index values of 3 or 4 [21]. Such

observations will need to be considered in real-world studies of ruxolitinib cream in patients with AD.

Ruxolitinib cream improves several signs and symptoms of AD that may contribute to the observed improvements in work productivity. As demonstrated in the TRuE-AD clinical trials, application of ruxolitinib cream alleviates pruritus [12]. In addition, preliminary data from the TRuE-AD trials showed that ruxolitinib cream improved skin pain [22] and provided a clinical benefit regardless of the anatomic region (including head and neck, trunk, upper limbs, and lower limbs) [23]. Ruxolitinib cream may also improve sleep, as measured by a ≥ 6-point improvement from baseline in the Patient-Reported Outcomes Measurement Information System (PROMIS) sleep disturbance questionnaire in the TRuE-AD1 study, although improvements in the PROMIS questionnaire were not statistically significant in the identically designed TRuE-AD2 study [12]. Itch and skin pain in patients with moderate or severe AD correlate with severity of sleep disturbance, which contributes to impairments in work productivity [24, 25]. Pruritus has also been directly correlated with impaired concentration, resulting

Fig. 1 Change from baseline in Work Productivity and Activity Impairment Questionnaire-Specific Health Problem version 2.0 (WPAI:SHP v2.0) scores for domains of (A) absenteeism, (B) presenteeism, (C) overall work impairment, and (D) daily activity impairment. CI confidence interval, * $p < 0.05$ versus vehicle; **** $p < 0.0001$ versus vehicle



in increased presenteeism in patients with AD, which may be a greater problem than absenteeism [26, 27]. Patients with AD experiencing fatigue, daytime sleepiness, and/or insomnia reported greater absenteeism than those with either AD or fatigue alone [4]. Finally, involvement in readily visible areas of the body, such as the face, is associated with impaired quality of life, which is in turn associated with indirect costs [28]. Additionally, patients with chronic hand eczema, another inflammatory skin condition, incur a substantial impairment in work productivity [29]. Managing physicians may promote the maintenance of or improvements in their patients' work productivity by screening for these signs and symptoms and tailoring their treatment strategy accordingly.

Previous studies reported an increased work impairment and indirect costs among patients with AD. In a recent survey of patients receiving topical therapy for moderate to severe AD, those with uncontrolled disease had a greater overall work impairment than those who had controlled disease [30]. Notably, patients from this survey and responders with mild to moderate AD in another survey reported a less severe overall work impairment compared with patients at baseline in the current study [5, 30]. A recent claims analysis of commercial-insured and Medicare-insured adults in the USA found that work absences and short-term disability claims were more common among patients with AD compared with matched controls without AD, contributing to higher indirect costs [31]. These real-world data support previous estimates, which were also calculated using

the human capital approach of estimating future loss of income, of increased indirect costs due to absenteeism and presenteeism in adults with uncontrolled AD compared with controlled AD [32] and in patients with AD compared with matched non-AD control patients [26]. In the current analysis, which included a population of patients of whom approximately 90% had been receiving active treatment and not achieved control prior to the study, estimated indirect costs were substantially reduced in patients with AD who applied ruxolitinib cream. These estimates were lower than estimated reductions in indirect costs in patients with moderate to severe AD treated with abrocitinib, even though an improvement in the overall work impairment was similar, indicating that the increased severity of the population in that analysis may have influenced the baseline indirect costs and that use of the overall annual median wage from the first quarter of 2020 and the lack of interim timepoints may have overestimated indirect costs [17].

This analysis had several limitations to consider. The data were from randomized controlled trials with a specified population and may not be reflective of real-world experiences. In particular, the trial design excluded patients with severe AD as indicated by a greater IGA score (> 3) or affected body surface area ($> 20\%$), a population that tends to be more resistant to therapy [33]. Extrapolation from the short-term vehicle-controlled period to annual costs may not account for potential AD disease progression in which ruxolitinib cream may no longer be effective. Furthermore, because of the limited data on the use of topical agents in

Table 3 WPAI:SHP v2.0 scores for overall work impairment

WPAI:SHP v2.0 score, mean (SD), %	Vehicle (<i>n</i> = 244)		0.75% Ruxolitinib cream (<i>n</i> = 483)		1.5% Ruxolitinib cream (<i>n</i> = 481)	
	<i>n</i>	Score	<i>n</i>	Score	<i>n</i>	Score
Absenteeism						
Baseline	136	5.2 (15.4)	269	7.9 (20.5)	273	3.9 (13.4)
Week 2	109	9.0 (21.3)	224	6.0 (17.6)	232	4.5 (14.8)
Week 4	96	13.2 (25.9)	219	7.7 (19.8)	239	6.9 (18.5)
Week 8	99	12.7 (21.3)	218	7.7 (21.5)	229	7.5 (19.1)
Presenteeism						
Baseline	135	33.9 (27.4)	267	30.1 (25.6)	272	29.8 (24.1)
Week 2	107	28.0 (25.7)	221	14.6 (18.6)	231	14.7 (19.9)
Week 4	92	23.2 (26.0)	215	11.9 (17.0)	236	10.1 (17.1)
Week 8	99	22.0 (24.3)	213	10.1 (17.3)	227	9.5 (17.1)
Overall work impairment						
Baseline	135	36.4 (28.3)	267	33.6 (27.9)	272	31.8 (25.4)
Week 2	107	32.4 (27.8)	221	18.0 (22.4)	231	17.8 (22.9)
Week 4	92	29.4 (29.2)	215	16.8 (21.6)	236	14.7 (22.0)
Week 6 ^a	NA	30.2 (NA)	NA	15.6 (NA)	NA	15.1 (NA)
Week 8	99	31.0 (27.9)	213	14.3 (22.3)	227	15.5 (22.8)
Daily activity impairment						
Baseline	243	33.2 (27.6)	483	31.3 (27.2)	479	32.2 (26.9)
Week 2	223	27.5 (26.5)	457	16.5 (21.5)	455	13.3 (18.1)
Week 4	205	23.8 (24.6)	452	12.3 (18.3)	456	10.8 (17.8)
Week 8	201	22.3 (25.3)	427	10.5 (17.6)	444	10.5 (17.5)

NA not available, *SD* standard deviation, *WPAI:SHP v.2.0* Work Productivity and Activity Impairment Questionnaire-Specific Health Problem version 2.0

^aWeek 6 overall work impairment data points were imputed by taking the mean of week 4 and week 8; these data were used in the economic model

Table 4 Estimated indirect costs incurred per employed patient during the 8-week trial period

Time period	Indirect cost per period, \$		
	Vehicle	0.75% Ruxolitinib cream	1.5% Ruxolitinib cream
Weeks 0–2	569	525	497
Weeks 2–4	507	281	278
Weeks 4–6	460	263	230
Weeks 6–8	472	243	236

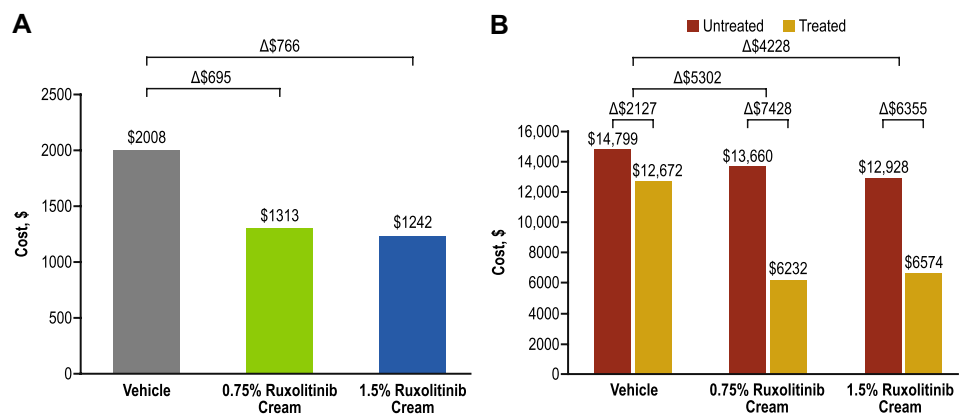
AD treatment, indirect cost comparisons were made versus vehicle rather than an active topical agent. This potentially overestimates the cost savings with ruxolitinib cream compared with other topical therapies. Additionally, only 56.1% of patients in our study completed the work-related questions, likely reflecting the proportion of the study population in employment and potentially providing an underestimation

of the work-related impairment when considering AD may prevent some people from working. Additionally, there was a drop-off in WPAI:SHP completion over the 8-week study period, with approximately 80% of patients applying ruxolitinib cream completing the baseline questionnaire at week 8. This drop-off may have led to an underestimation of productivity loss as the worst affected patients may not have completed the questionnaire in later weeks. Furthermore, the model used does not account for all indirect costs, such as impaired quality of life. Finally, this analysis focuses only on indirect costs, without consideration of direct medical and pharmacy costs, including the cost of ruxolitinib cream.

5 Conclusions

In summary, ruxolitinib cream is associated with significantly improved work productivity and daily activity compared with vehicle for patients with AD. Patients randomized to ruxolitinib cream reported reduced work time

Fig. 2 Total estimated indirect costs in 2021 US dollars incurred per patient (A) over the 8-week trial period and (B) annualized



missed, work impairment, and daily activity impairment compared with vehicle. Results of the indirect cost analysis showed that ruxolitinib cream may also significantly reduce the annual indirect cost burden on patients with AD.

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Declarations

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Conflicts of Interest/Competing Interests Lisa Bloudek, Kristen Migliaccio-Walle, and Sean D. Sullivan are employees of Curta Inc. and served as paid consultants to Incyte Corporation in connection with this study. Lawrence F. Eichenfield has served as an investigator, consultant, speaker, or data safety monitoring board member for AbbVie, Ammirall, Arcutis, Asana BioSciences, Dermavant, Eli Lilly, Forte Biosciences, Galderma, Ichnos/Glenmark, Incyte Corporation, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Otsuka, Pfizer, Regeneron, and Sanofi Genzyme. Jonathan I. Silverberg has received honoraria for advisory board, speaker, and consultant services from AbbVie, Asana, Bluefin, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Glenmark, Incyte Corporation, Kiniksa, LEO Pharma, Menlo, Novartis, Pfizer, Realm, Regeneron, and Sanofi; and research grants for investigator services from GlaxoSmithKline and Galderma. Vijay N. Joish, Jennifer H. Lofland, and Kang Sun are employees and shareholders of Incyte Corporation. Matthias Augustin has served as a consultant, researcher, and/or has received research grants from AbbVie, ALK-Abelló, Ammirall, Amgen, Bayer, Beiersdorf, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Centocor, Dermira, Eli Lilly, Galderma, Genzyme, GlaxoSmithKline, Hexal, Janssen, LEO Pharma, Medac, Menlo Therapeutics, MSD, Mylan B.V., Novartis, Pfizer, Regeneron, Sandoz, Sanofi, Stallergenes, Trevi, and Xenoport. Sean D. Sullivan is an owner of VeriTech Corporation and served as a consultant to Incyte Corporation in connection with this study.

Ethics Approval The study was conducted in accordance with the International Council on Harmonisation Guideline for Good Clinical Practice, the Declaration of Helsinki, and all other applicable local ethical and legal requirements.

Consent to Participate Written informed consent or assent was provided by all patients before enrollment.

Consent to publish Not applicable.

Availability of Data and Material Incyte Corporation (Wilmington, DE, USA) is committed to data sharing that advances science and medicine while protecting patient privacy. Qualified external scientific researchers may request anonymized datasets owned by Incyte Corporation for the purpose of conducting legitimate scientific research. Researchers may request anonymized datasets from any interventional study (except phase I studies) for which the product and indication were approved on or after 1 January, 2020 in at least one major market (e.g., USA, European Union, Japan). Data will be available for request after the primary publication or 2 years after the study has ended. Information on Incyte Corporation's clinical trial data sharing policy and instructions for submitting clinical trial data requests are available at: <https://www.incyte.com/Portals/0/Assets/Compliance%20and%20Transparency/clinical-trial-data-sharing.pdf?ver=2020-05-21-132838-960>.

Code Availability Not applicable.

Authors' Contributions All authors contributed to the study conception and design and development of the manuscript. All authors read and approved the final manuscript.

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