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ORIGINAL ARTICLE

Nemolizumab in moderate to severe atopic dermatitis: An exploratory analysis of work productivity and activity impairment in a randomized phase II study

Ryosuke MIHARA,[1] Kenji KABASHIMA,[2] Masutaka FURUE,[3] Miwa NAKANO,[1] Thomas RUZICKA[4]

[1]*Chugai Pharmaceutical Co. Ltd, Tokyo,* [2]*Graduate School of Medicine, Kyoto University, Kyoto,* [3]*Graduate School of Medical Science, Kyushu University, Fukuoka, Japan,* [4]*Ludwig-Maximilian University, Munich, Germany*

ABSTRACT

Atopic dermatitis negatively impacts work productivity. This study investigated the impact of nemolizumab on work productivity and activity impairment in adults with moderate to severe atopic dermatitis inadequately controlled by topical treatments in a two-part, phase II, randomized control trial. The Work Productivity and Activity Impairment – Atopic Dermatitis questionnaire was an exploratory end-point. Part A was a 12-week, placebo-controlled study in which patients received s.c. nemolizumab 0.1, 0.5 or 2.0 mg/kg every 4 weeks or 2.0 mg/kg every 8 weeks. Part B was a 52-week extension in which all patients received active treatment. A total of 138 patients had Work Productivity and Activity Impairment – Atopic Dermatitis data; 104 were employed at baseline. At week 12, patients receiving nemolizumab every 4 weeks showed greater mean (standard error) Work Productivity and Activity Impairment – Atopic Dermatitis improvement (score reduction) from baseline versus placebo: Percent Work Time Missed (0.1, 0.5 or 2.0 mg/kg vs placebo): –4.0% (3.9%), –1.7% (4.2%) and –1.6% (4.2%) versus 4.9% (4.5%); Percent Impairment While Working, –15.8% (6.0%), –24.1% (6.5%) and –34.3% (6.4%) versus –16.5% (7.1%); Percent Overall Work Impairment, –16.3% (6.0%), –23.1% (6.5%) and –34.5% (6.3%) versus –16.6% (7.1%); and Percent Activity Impairment, –13.4% (5.3%), –23.5% (5.3%) and –41.9% (5.5%) versus –10.9% (5.7%). Improvements were sustained through week 64. Nemolizumab-treated patients with moderate to severe atopic dermatitis reported improvements in Work Productivity and Activity Impairment through week 64.

Key words: **atopic dermatitis, clinical trial phase II, nemolizumab, pharmacotherapy, skin diseases.**

INTRODUCTION

Atopic dermatitis (AD) is a chronic, inflammatory, T-cell-mediated skin disease associated with disseminated, intensely pruritic skin lesions. Itching, the dominant clinical feature of AD,[1–3] is mediated by the binding of the pro-inflammatory cytokine interleukin (IL)-31 to IL-31 receptor A on sensory neurones[4–6] and chronic pruritus exacerbates disease through the itch–scratch cycle.[7] Long-term symptom alleviation is a treatment goal for this chronic condition; however, treatment options are limited for patients with AD unresponsive to topical therapies, such as the corticosteroids and calcineurin inhibitors that form the mainstay of therapy.[3,8,9]

Atopic dermatitis negatively impacts health-related quality of life (HRQoL), sleep quality, mental health and work productivity,[10–12] with greater disease severity associated with greater work and activity impairment.[10,12,13] The effect of AD on mood and sleep disorders, HRQoL and work productivity has been reported to be similar to that of psoriasis;[12] however, the burden of illness in AD is still a relatively understudied area. Pruritus is a key contributor to the burden of AD, and continuous itching leads to loss of sleep, reduced HRQoL and symptoms of depression, as well as impacting daily functioning including the ability to work and study.[11,14]

Nemolizumab is an anti-IL-31 receptor A humanized monoclonal antibody that blocks IL-31-mediated signaling. In addition to stimulating pruritus, IL-31 also has a role in perpetuation of the inflammatory response and dysregulation of the physical and functional properties of the skin barrier,[5,15,16] both of which contribute to ongoing disease.

Correspondence: Ryosuke Mihara, M.S., Chugai Pharmaceutical Co. Ltd, 2-1-1 Nihonbashi-Muromachi, Chuo-ku, Tokyo 103-8324, Japan. Email: miharaus@chugai-pharm.co.jp

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Data sharing statement: We provide qualified researchers access to individual patient level data through the clinical study data request platform (www.clinicalstudydatarequest.com). Further details of Chugai's Data Sharing Policy are available here (www.chugai-pharm.co.jp/english/profile/rd/ctds_request.html).

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Nemolizumab demonstrated improvements in pruritus, disease severity and sleep disturbance in a phase II, 12-week, randomized, double-blind, placebo-controlled, dose-finding study (Part A) in adults with moderate to severe AD inadequately controlled by topical treatments (XCIMA study; NCT 01986933).[17] A double-blind, 52-week extension study (Part B) demonstrated that nemolizumab was associated with clinically meaningful reductions in pruritus and dermatitis when administrated for up to 64 weeks.[18] Nemolizumab was also well tolerated, with no new safety concerns identified with long-term use.[17,18] To date, work productivity in patients with AD has not been well studied. Therefore, the objective of the current post-hoc analysis was to investigate the effects of nemolizumab on work productivity and activity impairment (WPAI) in patients with moderate to severe AD in the 12-week, placebo-controlled study (Part A) and subsequent long-term extension (Part B) using the Work Productivity and Activity Impairment – Atopic Dermatitis (WPAI-AD) questionnaire as the assessment index. We also evaluated the relationship between WPAI and indicators of disease severity to identify clinical outcomes associated with ability to work and daily activity.

METHODS

Study design

Details of the study design have been reported previously.[17,18] Briefly, Part A was an evaluation of four nemolizumab dose regimens (0.1, 0.5 or 2.0 mg/kg s.c. every 4 weeks [Q4W] or 2.0 mg/kg s.c. every 8 weeks [Q8W]). In Part B, patients receiving nemolizumab in Part A continued the same dose and patients randomized to placebo in Part A were re-randomized to nemolizumab (0.1, 0.5 or 2.0 mg/kg Q4W) in a 1:1:1 ratio (re-randomized patients were not included in the current analysis).

The study was performed in accordance with the guidelines for Good Clinical Practice and the Declaration of Helsinki. All study documents and procedures were approved by the appropriate ethics committee and institutional review board (IRB) at each study center (IRB protocol approval no. QUI1-13-404; dated 28 October 2013 for site of principal investigator), and written informed consent was provided by all patients. The trial registration number is NCT 01986933.

Patients

Key inclusion criteria for Parts A and B have been described previously.[17,18] Eligible patients were 18–65 years of age with moderate to severe AD inadequately controlled by topical corticosteroids or topical calcineurin inhibitors, with an Eczema Area and Severity Index (EASI) score of 10 or more, pruritus visual analog scale (VAS) score of 50 mm or more and static Investigator's Global Assessment (sIGA) score of 3 or more. The WPAI-AD questionnaire was administrated to patients in the USA and Japan only, owing to limited availability of local language versions of the WPAI-AD questionnaire.[19] Patients were required to have available WPAI-AD data from baseline and subsequent visits to be eligible for the current analysis.

Study assessments

The WPAI – Specific Health Problem (WPAI-SHP) questionnaire,[19,20] developed to assess the impact of specific conditions on the ability to work and perform regular daily activities, was adapted for use in AD. The questionnaire has four domains: (i) Work Time Missed (absenteeism); (ii) Percent Impairment While Working (presenteeism); (iii) Percent Overall Work Impairment; and (iv) Percent Activity Impairment.[19,20] Percent overall work productivity loss is calculated based on absenteeism and presenteeism using the formula: absenteeism + (% of time worked × presenteeism). Notably, percent overall work impairment only targets the working population, while activity impairment targets both the working and non-working population.

When completing the WPAI-AD questionnaire, patients were asked to consider the last 7 days prior to the study visit. WPAI-AD (expressed as percentage of impairment, with higher numbers indicating greater impairment and lesser productivity) and Dermatology Life Quality Index (DLQI) (measured on a scale of 0–30, with higher scores representing greater impairment) were completed by patients every 4 weeks throughout the total study period (Parts A and B). Pruritus VAS (which ranges from 0 [no itch] to 100 mm [worst imaginable itch]) and sleep disturbance VAS (which ranges from 0 [no sleep loss] to 100 mm [inability to sleep at all]) were completed by patients once daily during Part A, and every 7 days during Part B. EASI (which ranges from 0–72, with higher scores indicating worse disease severity) was measured at each study visit during Parts A and B. On days with study visits, patient-reported outcome assessments were completed prior to other study assessments. Patients were evaluated by the same assessor at all visits for consistency (when possible) and assessor training was employed to minimize variation across study sites.

Study end-points

Work Productivity and Activity Impairment - Atopic Dermatitis was an exploratory end-point in the study; primary and secondary efficacy end-points have been previously described.[17,18] Briefly, the primary end-point was percentage improvement from baseline in pruritus VAS score, and secondary end-points included changes from baseline in EASI score, SCORing Atopic Dermatitis score, sIGA, body surface area affected by AD and sleep disturbance VAS.

Statistics

Analyses were performed in the WPAI-AD subgroup of the intent-to-treat (ITT) population (all randomized patients who received at least one dose of placebo or nemolizumab in Part A or B and had ≥1 post-dose efficacy assessment). All WPAI analyses were performed as described for the primary and secondary end-point analyses.[17] Patients enrolled into the exploratory arm (nemolizumab 2.0 mg/kg Q8W) and all data collected during or after rescue therapy were excluded from analyses of Part A. Missing data were imputed using the last observation carried forward method for analyses from Part A (placebo controlled). In analyses of the total study period

Table 1. Baseline demographics and disease characteristics (ITT population, WPAI-AD subgroup)

Characteristic	Placebo (*n* = 28)	Nemolizumab 0.1 mg/kg Q4W (*n* = 28)	Nemolizumab 0.5 mg/kg Q4W (*n* = 28)	Nemolizumab 2.0 mg/kg Q4W (*n* = 27)	Nemolizumab 2.0 mg/kg Q8W (*n* = 27)	Nemolizumab total (*n* = 110)
Patients, *n* (%)						
USA	12 (43)	12 (43)	12 (43)	11 (41)	12 (44)	47 (43)
Japan	16 (57)	16 (57)	16 (57)	16 (59)	15 (56)	63 (57)
Male sex, *n* (%)	14 (50)	13 (46)	14 (50)	18 (67)	11 (41)	56 (51)
Age, years	39 ± 13.0	32 ± 10.9	35 ± 11.1	38 ± 11.3	35 ± 12.5	35 ± 11.5
Weight, kg	73 ± 24.3	73 ± 25.2	73 ± 22.4	72 ± 17.0	70 ± 22.1	72 ± 21.6
Pruritus VAS, mm	78 ± 12.9	78 ± 11.2	77 ± 12.1	78 ± 11.1	78 ± 11.8	78 ± 11.4
EASI score	31 ± 16.1	35 ± 17.5	31 ± 18.5	31 ± 12.6	30 ± 16.1	32 ± 16.2
Body surface area affected, %	45 ± 31.5	57 ± 29.5	50 ± 30.9	59 ± 24.2	51 ± 29.3	54 ± 28.5
sIGA score, *n* (%)						
3	13 (46)	9 (32)	12 (43)	10 (37)	14 (52)	45 (41)
4	13 (46)	11 (39)	12 (43)	14 (52)	9 (33)	46 (42)
5	2 (7)	8 (29)	4 (14)	3 (11)	4 (15)	19 (17)
DLQI	15 ± 5	15 ± 6	14 ± 6	15 ± 6	15 ± 8	15 ± 6
Sleep disturbance VAS	65 ± 23	68 ± 21	65 ± 22	65 ± 23	66 ± 22	66 ± 22
WPAI-AD						
Employed, *n* (%)	20 (71)	20 (71)	22 (79)	19 (70)	23 (85)	84 (76)
Percent Work Time Missed†	1 ± 4.6	5 ± 8.8	12 ± 29.4	2 ± 5.8	11 ± 25.0	8 ± 20.6
Percent Impairment While Working†	52 ± 27.6	61 ± 26.8	53 ± 28.3	55 ± 25.3	51 ± 28.9	55 ± 27.1
Percent Overall Work Impairment†	53 ± 27.2	62 ± 26.0	53 ± 28.6	56 ± 25.1	53 ± 30.2	56 ± 27.4
Percent Activity Impairment	63 ± 23.6	69 ± 25.7	59 ± 27.5	62 ± 28.0	65 ± 29.0	64 ± 27.5

Data are reported as mean ± standard deviation, unless otherwise stated. †Patients employed at baseline. DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; ITT, intent-to-treat; Q4W, every 4 weeks; Q8W, every 8 weeks; sIGA, static Investigator's Global Assessment; VAS, visual analog scale; WPAI-AD, Work Productivity and Activity Impairment – Atopic Dermatitis.

(Parts A and B), all data during and after administration of rescue therapy were included and no data imputation was applied. Patients receiving nemolizumab 2.0 mg/kg Q8W were included in analyses of total study period only. Patients randomized to placebo in Part A were excluded from analyses of the total study period (Parts A and B). ANCOVA for each domain of WPAI individually, adjusted for baseline WPAI-AD score and region, was performed to estimate the least squares mean change from baseline in WPAI-AD scores at week 12 in the nemolizumab 0.1, 0.5 and 2.0 mg/kg Q4W groups versus the placebo group. As the analyses were exploratory, adjustments for multiple testing were not applied. To identify clinical outcomes which may correspond with work productivity in AD, Pearson correlation analysis was performed in patients receiving nemolizumab (0.1, 0.5 or 2.0 mg/kg Q4W) to assess the relationship between improvement from baseline at week 12 in WPAI-AD scores and improvement from baseline at week 12 in dermatitis score (EASI) or patient-reported outcomes (pruritus VAS, sleep disturbance VAS and DLQI). To further assess the impact of pruritus on work and activity impairment, WPAI-AD scores were evaluated in patients receiving nemolizumab Q4W (0.1, 0.5 or 2.0 mg/kg) with 50% or more improvement from baseline at week 12 in pruritus VAS score (high-responders) versus patients with less than 50% improvement from baseline at week 12 in pruritus VAS score (low-responders and non-responders). Statistical analyses were performed using SAS software, version 9.2 (TS2M3; SAS Institute, Cary, NC, USA).

Table 2. Change from baseline in WPAI at week 12

Parameter	Placebo (*n* = 28)	Nemolizumab 0.1 mg/kg Q4W (*n* = 28)	Nemolizumab 0.5 mg/kg Q4W (*n* = 28)	Nemolizumab 2.0 mg/kg Q4W (*n* = 27)
Percent Work Time Missed				
n	14	18	17	16
LSmean	4.93	−3.98	−1.72	−1.62
SE	4.48	3.91	4.15	4.17
P†		0.1387	0.2875	0.2892
Percent Impairment While Working				
n	13	18	15	16
LSmean	−16.48	−15.82	−24.12	−34.32
SE	7.08	5.99	6.51	6.35
P†		0.9438	0.4309	0.0666
Percent Overall Work Impairment				
n	13	18	15	16
LSmean	−16.58	−16.32	−23.14	−34.50
SE	7.07	5.97	6.49	6.32
P†		0.9778	0.4974	0.0646
Percent Activity Impairment				
n	22	26	25	24
LSmean	−10.86	−13.40	−23.50	−41.88
SE	5.69	5.27	5.34	5.46
P†		0.7446	0.1089	0.0002

†*P*-value compared with placebo. LSmean, least square mean; Q4W, every 4 weeks; Q8W, every 8 weeks; SE, standard error; WPAI, Work Productivity and Activity Impairment.

RESULTS

Patients

Participant flow through study Part A and Part B has been previously reported.[18] Of the 264 patients in the ITT population, 138 who received placebo or nemolizumab in Part A had available WPAI-AD data and were included in the current analysis (Table 1). Of these, 111 patients completed Part A, 95 participated in Part B and 59 completed Part B. Patient baseline demographics and clinical characteristics in the ITT WPAI-AD subgroup were similar to those of the overall study population,[17] and 104 patients were employed at baseline. While patients reported low baseline absenteeism (mean Percent Work Time Missed, range 1–12%), which was comparable with patients with moderate to severe AD and patients with other moderate to severe diseases (plaque psoriasis, rheumatoid arthritis and asthma) reported elsewhere,[10,21–23] they reported greater baseline presenteeism (mean Percent Overall Work Impairment, range 53–62%) and impairment when performing daily activities (mean Percent Activity Impairment, range 59–69%), suggesting a high burden of disease in this patient population.

Improvement from baseline in WPAI-AD scores

At week 12, patients receiving nemolizumab Q4W demonstrated greater least squares mean (standard error) decrease from baseline (i.e. improvement) in WPAI-AD scores compared with

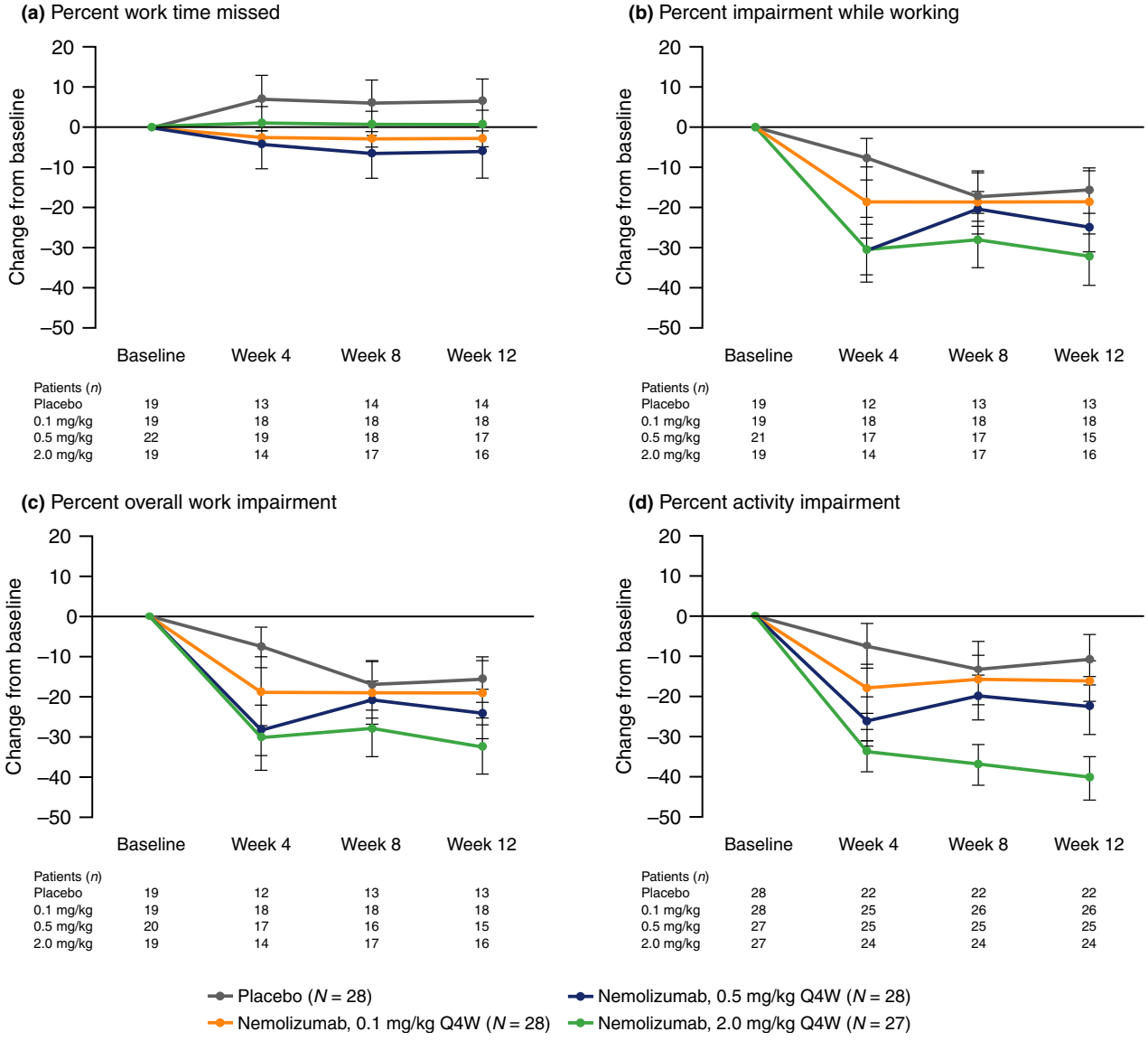

Figure 1. Change from baseline in WPAI-AD scores at weeks 4, 8 and 12 for nemolizumab compared with placebo. (a) Percent Work Time Missed. (b) Percent Impairment While Working. (c) Percent Overall Work Impairment. (d) Percent Activity Impairment. Data show mean ± standard error. Q4W, every 4 weeks; WPAI-AD, Work Productivity and Activity Impairment – Atopic Dermatitis.

patients receiving placebo (Table 2). Improvement from baseline in WPAI-AD scores was observed from week 4 (Fig. 1). Improvements in WPAI-AD work and activity impairment domain scores observed at week 12 were sustained up to week 64 in patients receiving nemolizumab Q4W and Q8W (Fig. 2).

Correlation between WPAI-AD and disease severity

Patients with available WPAI-AD data demonstrated improvement from baseline at week 12 in pruritus VAS, EASI, sleep disturbance VAS and DLQI, which are indicators of disease severity (Fig. 3). Pearson correlation analysis revealed a strong positive relationship between percent change from baseline at week 12 in WPAI-AD scores and that of pruritus VAS (WPAI-AD activity impairment and work domains, r = 0.53–0.75) and sleep disturbance VAS (WPAI-AD work and activity impairment domains, r = 0.64–0.70) (Fig. 4). Moderate positive correlations were also observed between percent change from baseline at week 12 in WPAI-AD scores and that of EASI (WPAI-AD work and activity impairment domains, r = 0.37–0.41) and DLQI (WPAI-AD activity impairment and work domains, r = 0.29–

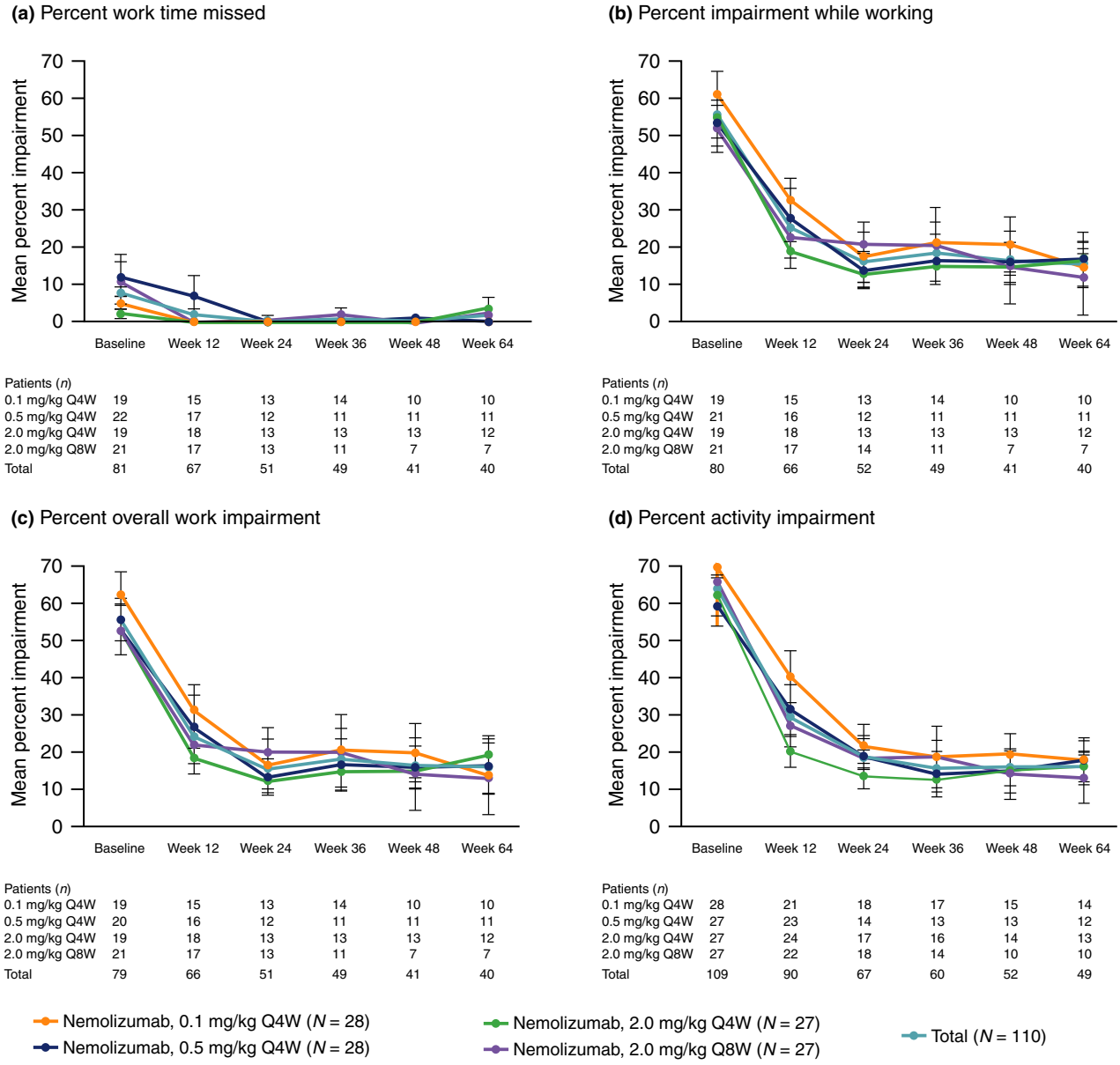

Figure 2. Absolute WPAI-AD scores at baseline and weeks 12, 24, 36, 48 and 64 for nemolizumab. Patients who were randomized to placebo in Part A of the study were excluded from analysis of the total period (Part A and B). (a) Percent Work Time Missed. (b) Percent Impairment While Working. (c) Percent Overall Work Impairment. (d) Percent Activity Impairment. Data show mean ± standard error. Q4W, every 4 weeks; Q8W, every 8 weeks; WPAI-AD, Work Productivity and Activity Impairment – Atopic Dermatitis.

0.34). Pearson correlation analysis of absolute change from baseline in WPAI-AD scores demonstrated a similar trend (Fig. S1).

Improvement from baseline in WPAI-AD scores in high-responders versus low-responders or non-responders

Of the 83 patients receiving nemolizumab Q4W (0.1, 0.5 or 2.0 mg/kg), 29 with work-related WPAI-AD data and 36 with general activity impairment data were defined as high-responders. A similar number of patients were considered low-responders or non-responders (26 and 38, respectively). High-responders demonstrated greater improvement in WPAI-AD scores across all four domains, compared with low-responders or non-responders (Fig. 5). Of the 28 patients receiving placebo, the number of patients considered high-responders was too low for meaningful comparison: four or less patients defined as high-responders; and 18 or less defined as low-responders or non-responders.

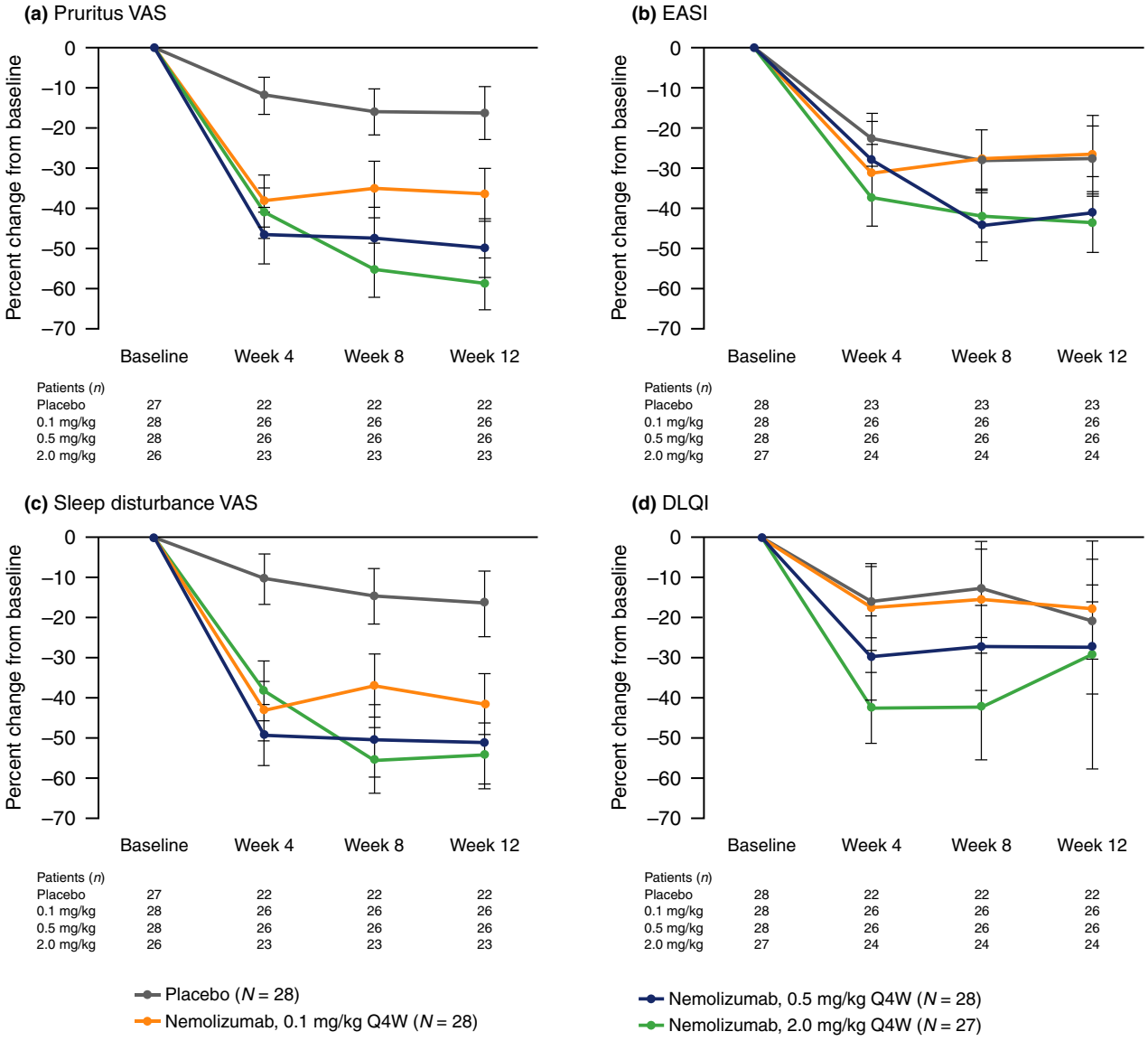

Figure 3. Percent change from baseline in pruritus VAS, EASI, sleep disturbance VAS and DLQI at weeks 4, 8 and 12 in patients with available WPAI data. (a) Pruritus VAS. (b) EASI. (c) Sleep Disturbance VAS. (d) DLQI. Data show mean ± standard error. DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; Q4W, every 4 weeks; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment.

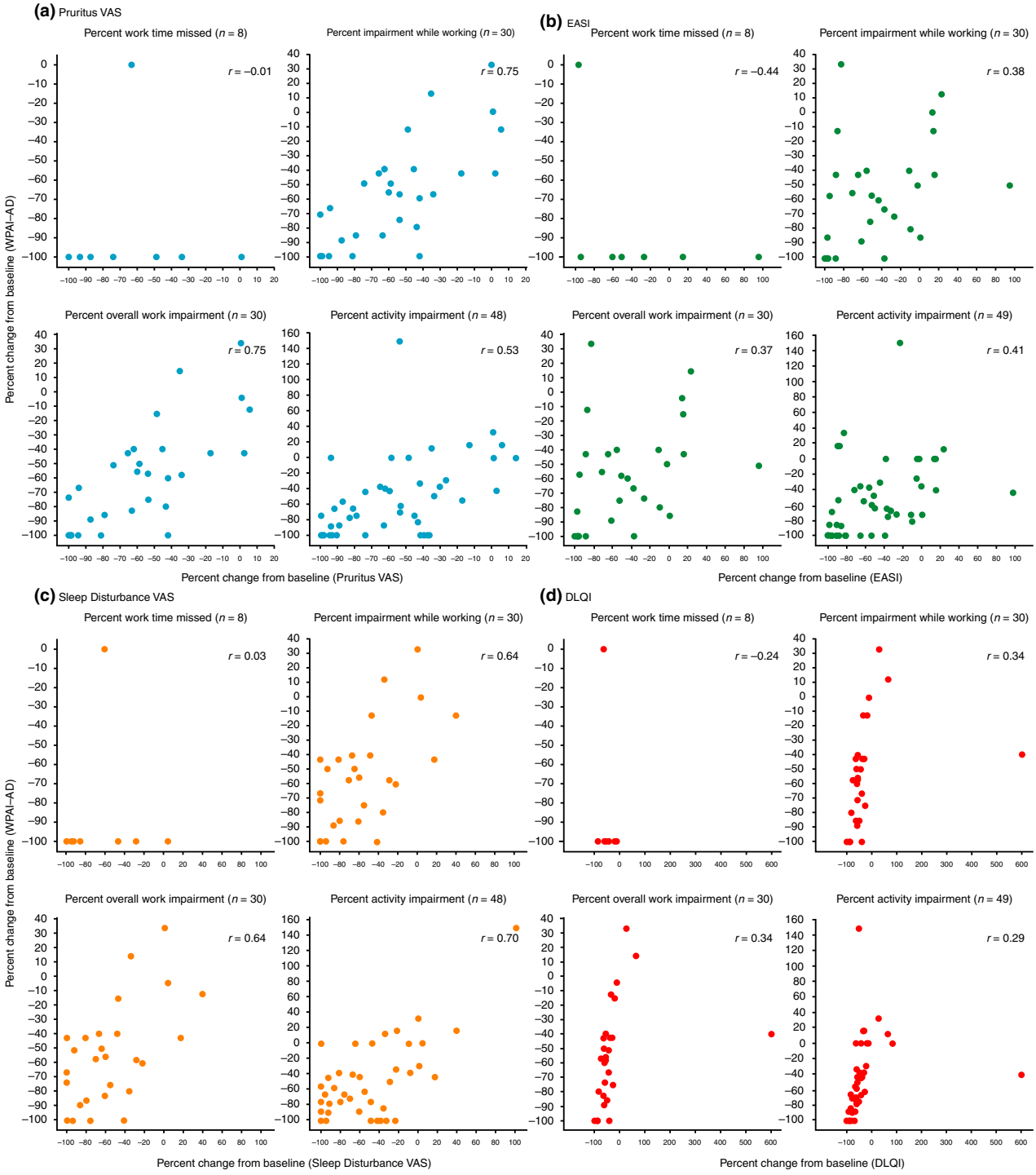

Figure 4. Pearson correlation to assess percent change from baseline at week 12 in WPAI-AD scores and percent change from baseline at week 12 in pruritus VAS, EASI, sleep disturbance VAS and DLQI scores in patients receiving nemolizumab 0.1, 0.5 or 2.0 mg/kg Q4W. (a) Pruritus VAS. (b) EASI. (c) Sleep Disturbance VAS. (d) DLQI. DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; Q4W, every 4 weeks; VAS, visual analog scale; WPAI-AD, Work Productivity and Activity Impairment – Atopic Dermatitis.

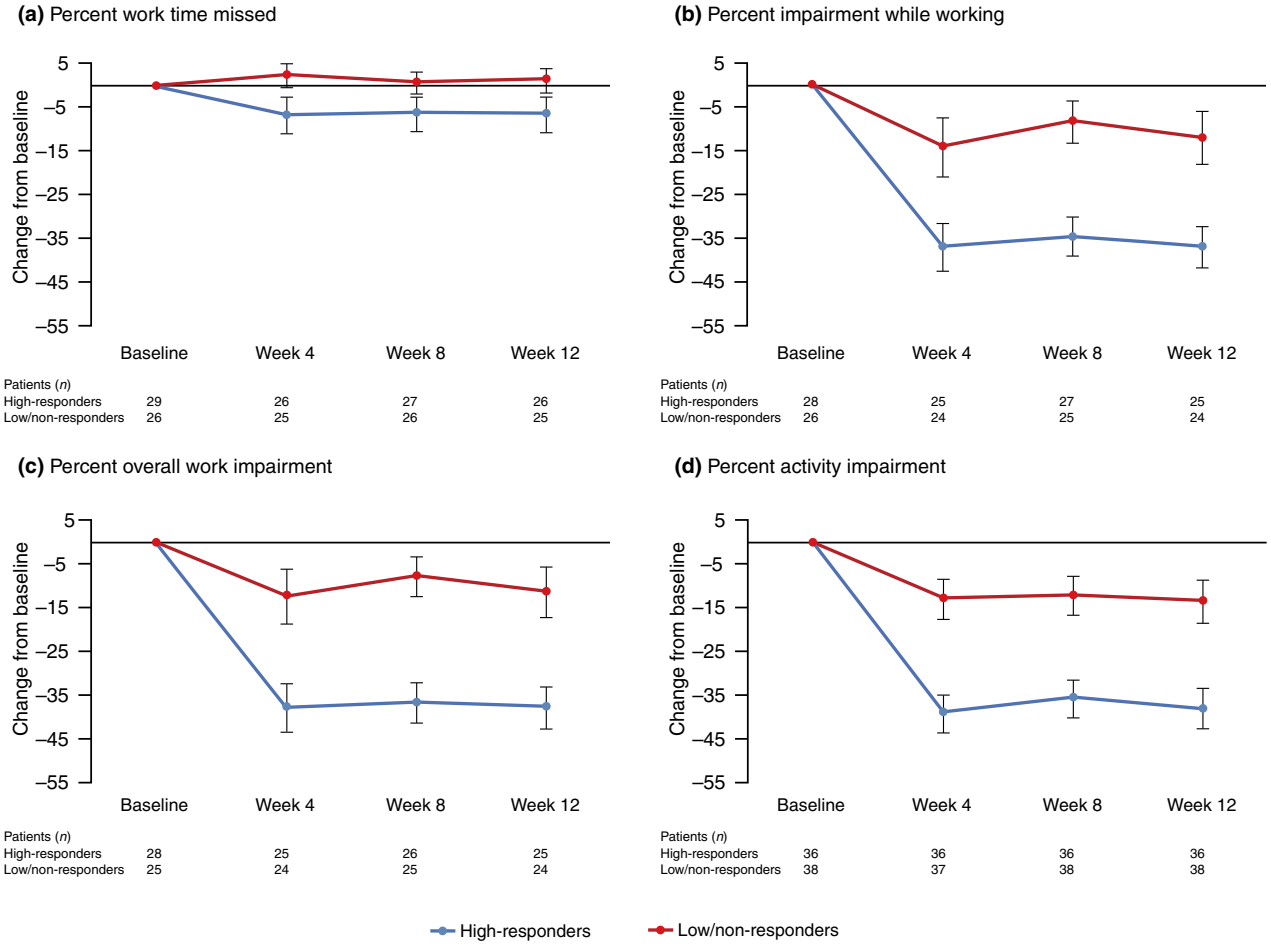

Figure 5. Change from baseline in WPAI-AD scores at weeks 4, 8 and 12 in high-responders (patients receiving nemolizumab Q4W with 50% or more improvement from baseline at week 12 in pruritus VAS score) and low-responders or non-responders. (a) Percent Work Time Missed. (b) Percent Impairment While Working. (c) Percent Overall Work Impairment. (d) Percent Activity Impairment. Data show mean ± standard error. Q4W, every 4 weeks; VAS, visual analog scale; WPAI-AD, Work Productivity and Activity Impairment – Atopic Dermatitis.

DISCUSSION

Nemolizumab-treated patients with moderate to severe AD reported numerically greater improvement in work productivity and ability to perform daily activities compared with patients receiving placebo in this 12-week, randomized phase II study. Improvement in the ability to perform non-work-related regular activities was most markedly observed for patients receiving nemolizumab 2.0 mg/kg Q4W versus placebo, although it should be emphasized that this was an exploratory analysis with no formal testing planned to compare groups; therefore, no inferences can be drawn from the statistical analyses. Overall, improvements in WPAI-AD were observed after 4 weeks of therapy and sustained for up to 64 weeks and our findings suggest that, of the AD symptoms evaluated here, pruritus and sleep disturbance most negatively impacted WPAI-AD. Disease severity and HRQoL also impaired WPAI-AD but to a lesser extent. These findings build on prior studies which demonstrate that pruritus, as the dominant symptom of AD, contributes to sleeplessness and reduced HRQoL in patients with AD.[11,14,24,25] As pruritus is a subjective symptom, it is difficult to distinguish the effect on other clinical outcomes, even in patients with significant improvement. Therefore, it is important to assess the effect on functional outcomes such as work productivity and daily activity. Our analysis identified significant improvement in high-responders in WPAI-AD scores across all four domains compared with low-responders which suggests that improvement in pruritus by nemolizumab can lead to preferable effects on other functional outcomes. This reinforces the importance of alleviating pruritus in AD and highlights the broader impact of the disease on patient functioning in the workplace and daily life.

In addition to the impact on HRQoL, skin disorders are associated with substantial economic burden. A comprehensive study into the economic impact of skin diseases in the USA estimated the overall annual cost of skin disorders in

2004 at $US39.3 billion.[26] This total included $US10.2 billion in lost productivity costs accounting for missed time from work to seek medical care, impaired ability to work and lost future earnings owing to premature death.[26] Patients with AD incur significantly greater health-care resource use and direct costs versus individuals without AD, with the cost burden rising with increasing disease severity.[27,28] While calculating the total direct and indirect costs of AD is challenging as it is a common disease with a broad spectrum of severity, the total annual financial burden associated with AD in the USA in 2004 was estimated at $US4.2 billion, the equivalent of $US5.3 billion in 2015.[26,29] This value does not include costs associated with presenteeism or work time missed due to reasons other than medical visits that are commonly associated with AD.[26,29] The same study reported the corresponding financial burden in 2004 associated with psoriasis at the lower cost of $US3.7 billion.[26,29] Using WPAI data from a phase III study investigating the impact of adalimumab on moderate to severe psoriasis, Kimball *et al*.[30] estimated the potential annual indirect cost savings for employers associated with reduction in work productivity impairment owing to psoriasis at approximately $US4500 per full-time employed patient, corresponding to an 11.1% improvement in work productivity impairment versus placebo, indicating the potential productivity benefits for patients with AD.

Presenteeism is a major contributor to productivity loss, with evidence to suggest it has a greater economic impact than absenteeism.[31–33] Our patients reported high levels of presenteeism at baseline; more than half of their work productivity and daily activities were impaired compared with those in prior studies of moderate to severe AD and other moderate to severe skin disorders,[10,21,34] suggesting a high burden of disease. Patients with high levels of impairment may therefore have the potential to derive economic benefits associated with nemolizumab therapy and the alleviation of pruritus.

The study has a number of limitations to consider when evaluating the findings. These include the small sample size and the absence of a placebo arm in Part B, which might have introduced bias owing to administration of only active drug. The WPAI-AD was only assessed in the USA and Japan and may not be generalizable to patients from other countries. A difference in work culture between Japan and the USA may have also impacted study findings. Patient-reported absenteeism and presenteeism were not validated against employment records, and information regarding employment status (full-time, part-time, job type) was unavailable.

In summary, nemolizumab-treated patients with moderate to severe AD inadequately controlled by topical treatments reported sustained improvements in work productivity and daily activities. Nemolizumab-associated improvement in pruritus and pruritus-associated sleep disturbance could lead to reduced productivity-related burden in AD.

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CONFLICT OF INTEREST: R. M. is an employee of Chugai Pharmaceutical Co. Ltd and owns stock in that company. K. K., M. F. and T. R. are consultants for Chugai Pharmaceutical Co. Ltd and have received honoraria. M. N. is an employee of Chugai Pharmaceutical Co. Ltd. M. F. is the Editor of the *Journal of Dermatology*.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. Pearson correlation to assess absolute change from baseline at week 12 in WPAI-AD scores and percent change from baseline at week 12 in pruritus VAS, EASI, sleep disturbance VAS and DLQI scores in patients receiving nemolizumab 0.1, 0.5 or 2.0 mg/kg Q4W. (a) Pruritus VAS. (b) EASI. (c) Sleep disturbance VAS. (d) DLQI. DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; Q4W, every 4 weeks; VAS, visual analog scale; WPAI-AD, Work Productivity and Activity Impairment – Atopic Dermatitis.

Table S1. List of investigators in the USA and Japan