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ORIGINAL RESEARCH

Efficacy of Dupilumab in Atopic Dermatitis: The Patient's Perspective

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ABSTRACT

Introduction: Atopic dermatitis (AD), a predominantly type 2 inflammatory skin disease, affects approximately 2–5% of adults, with a high burden of disease. In moderate-to-severe AD, lesions can be extensive and pruritus intense with patients experiencing skin pain, sleep and mental health disturbances, and diminished quality of life (QoL).

Methods: The objective of this study was to evaluate the efficacy of dupilumab for the treatment of AD from the patients' perspective using patient-reported outcome data from four clinical trials (CHRONOS, SOLO 1&2, and CAFÉ) in patients ($N = 1553$) receiving either the approved 300 mg q2w dupilumab with/without topical corticosteroids (TCS) dose or control (placebo or placebo + TCS). Patient Global Assessment of Disease Status (PGADS) was used to measure patients' well-being and Patient Global Assessment of Treatment Effect (PGATE) was used to measure treatment efficacy. Patients were asked "Considering all the ways in which your eczema affects you, indicate how well you are doing" to assess their perception of well-being and "How would you rate the way your eczema responded to the study medication?" to assess their perception of treatment effect. Possible responses for both metrics included poor, fair, good, very good, and excellent.

Results: In all four studies, a significantly higher proportion of dupilumab-treated patients reported "Good"/"Very Good"/"Excellent" disease status from week 2 through study

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end versus control (CHRONOS, 52 weeks: 69.8% vs. 25.1%; SOLO 1&2, 16 weeks: 59.5% vs. 24.6%; CAFÉ, 16 weeks: 84.1% vs. 45.4%; all $P < 0.0001$), and significantly more dupilumab-treated patients reported "Good"/"Very Good"/"Excellent" treatment efficacy versus control (CHRONOS: 72.6% vs. 24.8%; SOLO 1&2: 65.0% vs. 21.1%; CAFÉ, 16 weeks: 85.0% vs. 36.1%; all $P < 0.0001$).

Conclusion: Adult patients with AD perceived that dupilumab with/without concomitant TCS was highly efficacious and improved overall disease status and well-being as early as week 2 and throughout treatment periods up to 1 year.

Keywords: Atopic dermatitis; Dupilumab; Patient perception; Patient-reported outcomes; Treatment efficacy

Key Summary Points

Why carry out this study?

Recent guidelines for the treatment of atopic dermatitis (AD) established that the patient's assessment should be taken into account in defining treatment response; however, some studies have shown discord between the physician's and the patient's assessment of disease.

What did the study ask?

How do patients perceive the efficacy of dupilumab for the treatment of AD?

What were the study outcomes/conclusions?

Adult patients with AD perceived that dupilumab, with or without concomitant topical corticosteroid treatment, was highly efficacious and improved overall disease status and well-being as early as week 2 and throughout treatment periods up to 1 year.

What has been learned from the study?

Overall, these study results indicate that most adult patients with AD perceive that dupilumab treatment is effective and improves well-being.

DIGITAL FEATURES

This article is published with digital features, including a video abstract, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.16677529.

INTRODUCTION

Atopic dermatitis (AD), a predominantly type 2 inflammatory skin disease characterized by pruritus (itch) and eczematous lesions, affects approximately 2–5% of adults [1, 2]. In moderate-to-severe AD, lesions can be extensive with intense pruritus and patients suffer with skin pain, sleep and mental health disturbances, and diminished quality of life (QoL) [3–5]. As a result of the chronic and relapsing nature of moderate-to-severe AD, patients often require long-term, ongoing systemic treatment.

Dupilumab, a fully human monoclonal antibody, specifically binds to interleukin (IL)-4 receptor alpha and inhibits signalling of IL-4 and IL-13, two important type 2 inflammatory cytokines [1, 6]. In clinical trials, dupilumab consistently improved clinical signs and symptoms of AD versus placebo, had an acceptable safety profile, and was shown to improve measures of sleep and QoL [7–15]. On the basis of the results of these trials, dupilumab is approved in the USA for adult and pediatric patients aged 6 years and above with moderate-to-severe AD not adequately controlled with topical therapies or when those therapies are not advisable [16]. It is also approved in Europe for the treatment of moderate-to-severe AD in patients 12 years and older, and severe AD in children 6–11 years old who are candidates for systemic therapy [17, 18].

Patients' perceptions of their treatment benefit are becoming increasingly important in the benefit/risk assessment of therapeutic agents. A recently published international treat-to-target consensus to guide the use of systemic treatment in adults with moderate-to-severe AD [19] established the patient's assessment of AD as an essential component in defining treatment response. The need to include the patient

perspective when making treatment decisions was also highlighted by a study suggesting a potential discord between physician-assessed and patient-reported levels of AD disease severity and burden [20, 21]. The objective of the current study was to evaluate the efficacy of dupilumab for the treatment of AD from the patient perspective using patient-reported outcome data from four randomized double-blind placebo-controlled clinical trials.

METHODS

This was a combined analysis of patient-reported treatment efficacy and disease-improvement data from four phase 3 randomized, placebo-controlled trials of dupilumab in adult patients with AD (CHRONOS [10], LIBERTY AD SOLO 1 [9], SOLO 2 [9], and CAFÉ [13]). Detailed methods for all studies, including full inclusion and exclusion criteria, have been previously reported. Briefly, patients from all studies were aged 18 years and older, with moderate-to-severe AD (Investigators Global Assessment score 3 or 4) inadequately controlled by topical corticosteroids (TCS) or cyclosporin A (CAFÉ only). Patients received dupilumab 300 mg or placebo once weekly (qw) or once every 2 weeks (q2w) and were followed up for 16 (SOLO and CAFÉ) or 52 (CHRONOS) weeks. Patients in the CHRONOS and CAFÉ studies also received concomitant TCS. Study design differences between CHRONOS (52 weeks), SOLO 1, SOLO 2, and CAFÉ (all 16 weeks) did not allow for pooling of data; however, as SOLO 1 and SOLO 2 were of identical design, data from these two studies were pooled (SOLO 1&2). All trials were approved by respective institutional review boards and conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, the International Conference on Harmonisation Good Clinical Practice guidelines, and applicable regulatory requirements. All patients or carers provided written informed consent before participating in the trial.

Patients' assessments of treatment efficacy and disease improvement for both dupilumab monotherapy (SOLO) and concomitant TCS therapy (CHRONOS and CAFÉ) were included in the analysis, using two widely used, but unvalidated, metrics: Patient Global Assessment of Disease Status (PGADS) measures static disease severity and Patient Global Assessment of Treatment Effect (PGATE) measures dynamic treatment efficacy. For PGADS, patients rated their overall well-being based on a 5-point Likert scale from "Poor" to "Excellent". Patients were asked: "Considering all the ways in which your eczema affects you, indicate how well you are doing." Response choices were "Poor" (1), "Fair" (2), "Good" (3)," "Very Good" (4), and "Excellent" (5). For PGATE, patients rated their opinion and perceived treatment effect. Patients were asked "How would you rate the way your eczema responded to the study medication?" Ratings were on a 5-point Likert scale of "Poor" (1), "Fair" (2), "Good" (3), "Very good" (4), or "Excellent" (5).

Study outcomes included the proportion of patients achieving a good/very good/excellent response in PGADS and PGATE over time and at weeks 16 and 52.

The study population was the full analysis set (FAS) which included all randomized patients. Only dosing regimens from the approved 300 mg q2w treatment and control (placebo or placebo + TCS) groups are reported.

RESULTS

Patients

For the 1553 patients included in this combined analysis, baseline demographics and disease characteristics were balanced between treatment groups and across studies (Table 1). Patients had a median age of 30–40.5 years and had chronic AD (median duration of disease 25.5–29 years; Table 1). Approximately half of patients across all of the studies had severe AD according to Investigator's Global Assessment ([IGA] patients with IGA 4, 46.7–50.0%; Table 1).

Table 1 General baseline demographics and disease characteristics

	CHRONOS [10]		SOLO 1&2 [15]		CAFÉ [13]	
	Placebo + TCS (*n* = 315)	Dupilumab 300 mg q2w + TCS (*n* = 106)	Placebo (*n* = 460)	Dupilumab 300 mg q2w (*n* = 457)	Placebo + TCS (*n* = 108)	Dupilumab 300 mg q2w + TCS (*n* = 107)
Age, median (IQR), years	34.0 (25.0–45.0)	40.5 (28.0–49.0)	37.0 (26.0–49.0)	36.0 (27.0–47.0)	37.5 (29.0–49.0)	38.0 (25.0–47.0)
Sex, male, *n* (%)	193 (61)	62 (58)	250 (54.3)	267 (58.4)	68 (63.0)	65 (60.7)
Race, White, *n* (%)	208 (66)	74 (70)	302 (65.7)	320 (70.0)	104 (96.3)	104 (97.2)
AD duration, median (IQR), years	26.0 (17.0–38.0)	28·0 (20.0–44.0)	27.0 (19.0–39.0)	25.5 (17.0–38.0)	28.5 (19.5–40.0)	29.0 (19.0–43.0)
EASI, median (IQR)	29.6 (22.2–40.8)	30.9 (22.3–41.6)	31.1 (22.2–42.6)	29.7 (21.1–40.5)	31.7 (24.2–40.7)	31.6 (25.2–39.2)
BSA, median (IQR), %	55.0 (40.0–75.0)	58.8 (43.5–78.5)	54.5 (36.0–75.0)	51.0 (36.5–71.0)	53.0 (38.3–69.3)	55.0 (44.0–66.0)
Patients with IGA 4 (severe), *n* (%)	147 (47)	53 (50)	225 (48.9)	223 (48.8)	52 (48.1)	50 (46.7)
Peak pruritus NRS score, median (IQR)	7.6 (6.3–8.6)	7.7 (6.6–8.5)	7.7 (6.4–8.7)	7.7 (6.3–8.8)	6.9 (4.9–8.1)	7.0 (5.4–8.0)
SCORAD—total score, median (IQR)	64.1 (55.9–76.1)	69.7 (60.4–79.8)	68.5 (58.3–78.1)	66.6 (56.5–76.7)	67.5 (58.5–76.6)	66.7 (61.1–76.2)
POEM score, median (IQR)	20.0 (16.0–25.0)	21.0 (16.0–25.0)	22.0 (16.0–26.0)	21.0 (17.0–25.0)	19.0 (14.0–24.0)	20.0 (15.0–24.0)
DLQI score, median (IQR)	14.0 (9.0–20.0)	13.5 (8.0–20.0)	15.0 (9.0–21.0)	14.0 (9.0–20.0)	13.0 (7.0–19.5)	14.0 (8.0–22.0)
Total HADS score, median (IQR)	11.0 (6.0–18.0)	12.5 (7.0–18.0)	12.0 (7.0–18.0)	13.0 (7.0–18.0)	13.0 (6.0 –18.5)	13.0 (6.0–19.0)

AD atopic dermatitis, *BSA* body surface area, *DLQI* Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *HADS* Hospital Anxiety & Depression Scale, *IGA* Investigator's Global Assessment, *IQR* interquartile range, *NRS* numerical rating scale, *POEM* Patient-Oriented Eczema Measure, *q2w* once every 2 weeks, *SCORAD* Scoring Atopic Dermatitis, *TCS* topical corticosteroids

Patient Global Assessment of Disease Status (PGADS)

In all four studies, a significantly higher proportion of dupilumab-treated patients reported a "Good"/"Very Good"/"Excellent" disease status at end of study versus control (16 weeks, SOLO 1&2: 59.5% vs. 24.6%; CAFÉ: 84.1% vs. 45.4%; 52 weeks, CHRONOS: 69.8% vs. 25.1% all $P < 0.0001$) (Fig. 1). A significant difference in patients' perceptions of AD improvement for the dupilumab versus control group was seen by week 2 in all studies that continued increasing until week 6 (all studies, $P < 0.0001$) and was maintained until the end of all four studies (Fig. 2).

Patient Global Assessment of Treatment Effect (PGATE)

Significantly more dupilumab-treated patients reported treatment effect as "Good"/"Very Good"/"Excellent" at the end of all four studies versus control (16 weeks, SOLO 1&2: 65.0% vs. 21.1%; CAFÉ: 85.0% vs. 36.1%; 52 weeks, CHRONOS: 72.6% vs. 24.8%; all $P < 0.0001$) (Fig. 3). As with PGADS, a difference in patients' perceptions of treatment efficacy for dupilumab versus control was apparent by week 2 in all studies (Fig. 2). In general, this treatment difference continued to increase until week 6 (all studies, $P < 0.0001$) and was maintained until end of treatment (all studies, $P < 0.0001$) (Fig. 2).

DISCUSSION

In this combined analysis of patient-reported disease improvement (PGADS) and patient-reported treatment efficacy (PGATE) data from four randomized, double-blind, placebo-controlled, pivotal phase 3 trials [9, 10, 13, 15], adult patients with AD receiving dupilumab with/without TCS perceived greater improvements in disease status and treatment effect versus patients treated with control. Dupilumab-treated patients across all four studies perceived improvement of their AD as early as week 2 and this improvement was maintained through week 16 (SOLO 1&2, CAFÉ) and week 52 (CHRONOS). These results reflect those of previous publications demonstrating the

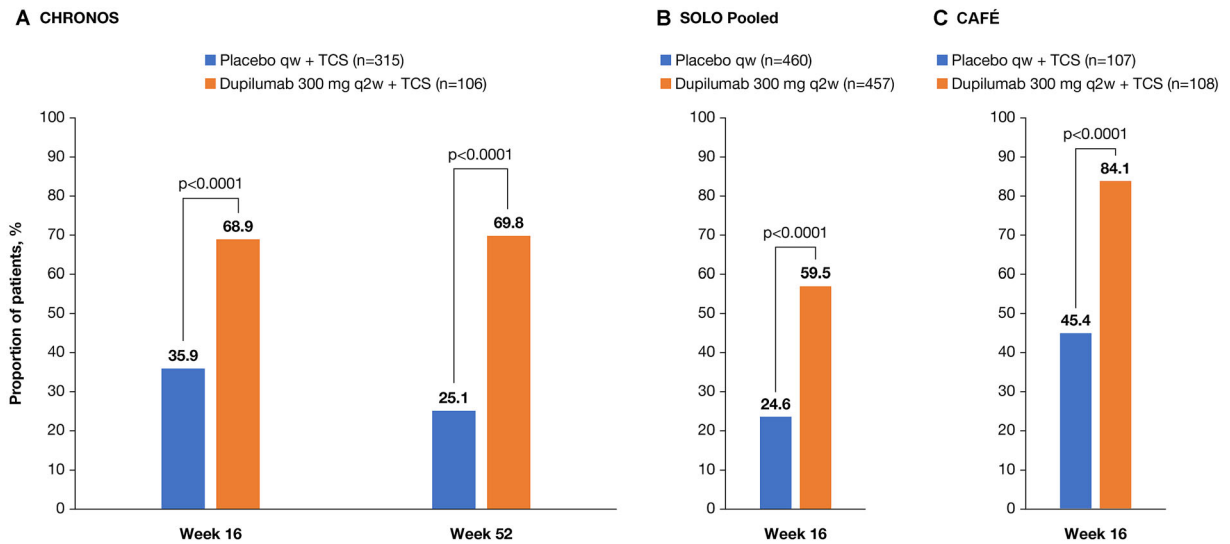

Fig. 1 Proportion of patients achieving good/very good/excellent response in PGADS at the end of study (week 16 and week 52[a]), FAS[b]. [a]Week 16 for CHRONOS, SOLO 1&2, and CAFÉ; week 52 for CHRONOS only; [b]Patient considered non-responder after rescue medication use. FAS full analysis sample, PGADS Patient Global Assessment of Disease Status, q2w once every 2 weeks, TCS topical corticosteroids

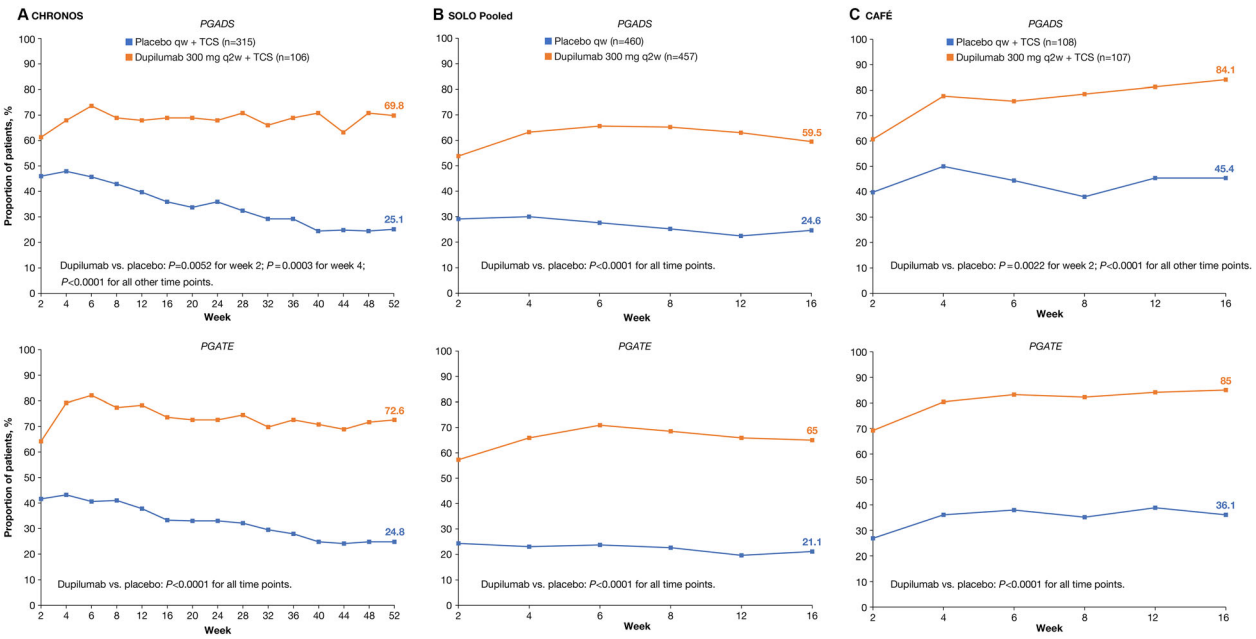

Fig. 2 Percentage of patients achieving good/very good/excellent response in PGADS and PGATE overtime, FAS[a,b]. [a]Week 16 for CHRONOS, SOLO 1&2, and CAFÉ; week 52 for CHRONOS only; [b]Patient considered non-responder after rescue medication use. FAS full analysis sample, PGADS Patient Global Assessment of Disease Status, PGATE Patient Global Assessment of Treatment Effect, q2w once every 2 weeks, TCS topical corticosteroids

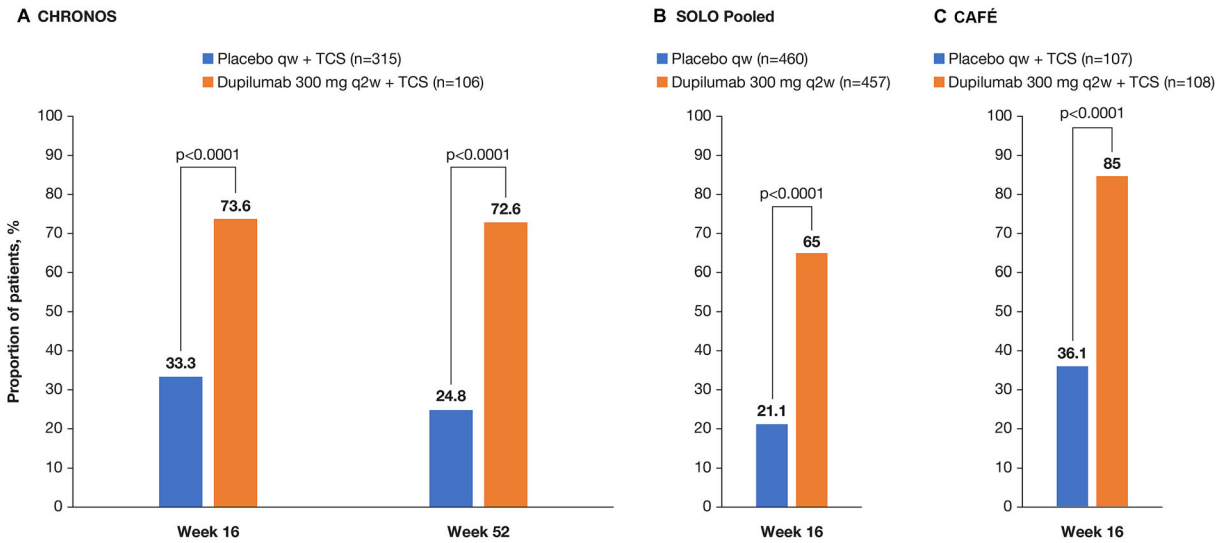

Fig. 3 Proportion of patients achieving good/very good/excellent response in PGATE at the end of study (week 16 and week 52[a]), FAS[b]. [a]Week 16 for CHRONOS, SOLO 1&2, and CAFÉ; week 52 for CHRONOS only; [b]Patient considered non-responder after rescue medication use. FAS full analysis sample, PGATE Patient Global Assessment of Treatment Effect, q2w once every 2 weeks, TCS topical corticosteroids

rapid and sustained effect of dupilumab using physician-assessed outcomes measures, as well as patient-reported peak pruritus and a range of holistic QoL measures capturing overall patient well-being (Dermatology Life Quality Index, DLQI; Hospital Anxiety & Depression Scale, HADS; Patient-Oriented Eczema Measure, POEM; and the 5-dimension 3-level EuroQol, EQ-5D) [7–15]. More importantly, the high percentage of patients reporting good perception of treatment effect (around 80% across studies) is similar to the percentage of patients who persist on treatment with dupilumab in real-world studies with up to 2 years of follow-up [22, 23]. In a retrospective cohort study of 1963 adult patients in the USA who received dupilumab treatment, the persistence (95% confidence interval [CI]) at 6 and 12 months was 91.9% (90.7–93.2%) and 77.3% (75.0–79.7%), respectively [23]. In the BioDay registry, which included 402 adult patients receiving dupilumab across multiple centers in the Netherlands, the overall drug survival rates for dupilumab were 91% and 88% after 1 and 2 years, respectively.

In a real-world cohort including 109 adults and children treated with dupilumab, the proportion (95% CI) of patients with persistence of remaining on dupilumab treatment at 12, 24, and 36 months was 96.5% (92.7–99.9%), 88.1% (83.9–98.5%), and 78.9% (64.4–99.9%), respectively [23]. Given that traditional clinical outcome measures used to evaluate AD [e.g., IGA and Eczema Area and Severity Index (EASI)] may not fully capture patient-reported burden [3, 20, 21], this analysis addresses an important gap in knowledge. These results provide insight into patient impressions of the efficacy of dupilumab for the treatment of moderate-to-severe AD and are a component of the holistic and meaningful improvement seen with dupilumab.

A potential limitation of this analysis is that it is based on data from clinical trials which may not be reflective of dupilumab use in a real-world setting. However, the results of this analysis are supported by recently published real-world data showing high persistence levels and low treatment discontinuation in patients treated with dupilumab for up to 3 years [22, 24, 25]. A further potential limitation of this analysis is that both measures used to assess disease status and treatment effect have not been formally validated.

CONCLUSION

Adult patients with moderate-to-severe AD treated with dupilumab with/without TCS perceived treatment as highly effective and as improving overall well-being, as early as 2 weeks and throughout treatment periods up to a year.

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Compliance with Ethics Guidelines. All trials were approved by respective institutional review boards and conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, the International Conference on Harmonisation Good Clinical Practice guidelines, and applicable regulatory requirements. All patients or carers provided written informed consent before participating in the trial.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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