Real-world treatment outcomes of systemic treatments for moderate-to-severe atopic dermatitis in children aged less than 12 years: 2-year results from PEDIatric STudy in Atopic Dermatitis

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Background: The arrival of biologics and small-molecule therapies (eg Janus kinase inhibitors) changed atopic dermatitis treatment, but older systemic treatments continue to be prescribed.

Objective: To provide real-world effectiveness, safety, and adherence data for dupilumab, cyclosporine, and methotrexate.

Methods: PEDIatric STudy in Atopic Dermatitis (NCT03687359) is a real-world, prospective, observational, 10-year study of children (<12 years) with inadequately controlled moderate-to-severe atopic dermatitis. We report 2-year interim results.

Results: Median treatment durations were 8.1, 13.0, and 10.7 months for dupilumab (n = 144), methotrexate (n = 114), and cyclosporine (n = 121), respectively. Dupilumab had numerically greater within-group improvements than methotrexate and cyclosporine in Eczema Area and Severity Index (−12.4* vs −5.7* and −3.3); body surface area affected (−19.9%* vs −11.8%* and −8.8%*); itching (nighttime: −2.1* vs −0.4 and + 0.1; daytime: −1.5* vs +0.1 and + 0.2; ≥6 years); itching/scratching (−3.6* vs −1.4* and −0.2; <6 years); and Patient-Oriented Eczema Measure (−7.0* vs −4.7* and −1.5) (*$P < .05$ within-group improvements from baseline). Dupilumab had less discontinuations (8.3% vs 28.9% and 43.0%) and adverse event(s) (18.1% vs 29.8% and 31.4%).

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IRB approval status: This study is being conducted in accordance with the principles established by the 18th World Medical Assembly and all subsequent amendments and in accordance with the guidelines for Good Epidemiology Practice. Each participating country has ensured that all the necessary local regulations are met. Ethics approval from an Institutional Review Board/Institutional Ethics Committee has been obtained in all countries currently participating in PEDIatric STudy in Atopic Dermatitis (PEDISTAD).

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Limitations: No randomization, placebo, or specified dosages.

Conclusion: Dupilumab was associated with numerically greater outcomes and higher adherence than cyclosporine or methotrexate. (J Am Acad Dermatol 2025;92:242-51.)

Key words: atopic dermatitis; cyclosporine; dupilumab; methotrexate; moderate-to-severe; pediatric; real-world; systemic.

INTRODUCTION

Atopic dermatitis (AD), a chronic, relapsing, inflammatory skin disease, often affects children. AD can cause intense itching, thus impacting sleep, mood, and the quality of life of patients and their families.[1] The prevalence of AD among children/adolescents varies globally from around 3% to 20%.[2,3] Patients with moderate-to-severe AD who do not respond to topical anti-inflammatory treatments have limited alternatives, including phototherapy and systemic immunosuppressants (particularly cyclosporine and methotrexate), which are used off-label for pediatric AD. Dupilumab is a systemic treatment that has been approved in the United States for moderate-to-severe AD from age 6 months[4] and in Europe for moderate-to-severe AD from 12 years and severe AD from 6 months.[5] Randomized controlled trials (RCTs) have shown that dupilumab significantly improves physician- and patient/caregiver-reported outcomes among patients of all ages with moderate-to-severe AD.[6-9] Of the newer Janus kinase inhibitors (JAKis), only baricitinib is approved in Japan for children aged <12 years.

The real-world PEDIatric STudy in Atopic Dermatitis (PEDISTAD) study enrolled children aged <12 years with inadequately controlled moderate-to-severe AD who received various treatments.[10,11] Here, we report interim physician- and patient/caregiver-reported outcomes, treatment discontinuation, and treatment-emergent adverse events (TEAEs) among children who received any of 3 systemic treatments of interest (dupilumab, methotrexate, or cyclosporine).

CAPSULE SUMMARY

- Before the recent arrival of targeted biologics (eg dupilumab), systemic immunosuppressants (eg methotrexate and cyclosporine) were commonly used to treat patients with moderate-to-severe atopic dermatitis.
- In this real-world setting, dupilumab treatment in pediatric patients (<12 years) was associated with numerically greater outcomes and higher adherence than methotrexate or cyclosporine.

METHODS

Study design

PEDISTAD (NCT03687359) is an ongoing, international, longitudinal, prospective, observational registry describing the disease characteristics, atopic comorbidities, and treatment patterns of pediatric patients with moderate-to-severe AD from Europe, Middle East, and Africa; North America; Latin America; and Asia-Pacific.[10,11] Patients were <12 years old (no minimum); had moderate-to-severe AD; were receiving systemic treatment (including biologics, cyclosporine, azathioprine, methotrexate, mycophenolate mofetil, corticosteroids, and ultraviolet therapy) for AD or topical treatment, but were otherwise candidates for systemic treatment because of a lack of adequate control and/or concern about the safety of long-term topical treatment; had signed informed consent from their caregiver; and gave age-appropriate patient assent.[10] Patients participating in an interventional clinical trial were excluded.

PEDISTAD is being conducted in accordance with the principles established by the 18th World Medical Assembly (and subsequent amendments) and the guidelines for Good Epidemiology Practice.[10] All necessary regulatory submissions were performed in accordance with local regulations and ethics approval was obtained.

Recruitment took place during September 2018 to May 2021 with a planned follow-up of 5 years. Interim baseline characteristics for the first 732 patients have already been reported.[11] Patients received various topical and systemic treatments (and doses) at the discretion of treating physicians,[10] which varied by region depending on availability and local practices. This interim analysis provides outcomes up to 2 years among patients who initiated dupilumab, methotrexate, or cyclosporine at study entry (baseline) or during the study. Other systemic treatments were not included due to low patient numbers.

Outcomes

All age-specific outcomes were assessed as change from therapy start to last available treatment

Abbreviations used:

AD:	atopic dermatitis
AE:	adverse event
BSA:	body surface area
CDLQI:	Children's Dermatology Life Quality Index
DFI:	Dermatitis Family Impact
EASI:	Eczema Area and Severity Index
IDQOL:	Infants' Dermatology Quality of Life Index
MedDRA:	Medical Dictionary for Regulatory Activities
PEDISTAD:	PEDIatric STudy in Atopic Dermatitis
POEM:	Patient-Oriented Eczema Measure
PT:	preferred term
RCT:	randomized controlled trial
TEAE:	treatment-emergent adverse event

observation. Physician-assessed outcomes were Eczema Area and Severity Index (EASI) (scale: 0-72) and affected body surface area (BSA) (0% to 100%). Two forms of the EASI scoring system were available depending on patient age (8 years and above or under 8 years). Patient/caregiver-reported outcomes were worst itching (previous night and current day; age ≥6 years) or worst scratching/itching (previous 24 hours; age <6 years) (0-10); Patient-Oriented Eczema Measure (POEM) (0-28); Children's Dermatology Life Quality Index (CDLQI) (age ≥4 years) or Infants' Dermatitis Quality of Life Index (IDQOL) (age <4 years) (0-30); and Dermatitis Family Impact (DFI) (0-30). Patient-reported outcomes (PROs) were adapted to patient age and caregivers were asked to administer or complete the PRO on behalf of their children depending on age. Worst itching was patient-reported by children ≥6 years old; CDLQI was patient-reported by children aged 3 to 11 years old with caregiver help; and worst scratching/itching, POEM, IDQOL, and DFI were caregiver-reported. For all scales, a higher score indicates more severe disease/impact.

Individual TEAEs affecting ≥1% of patients in any group by Medical Dictionary for Regulatory Activities (MedDRA) version 21.1 preferred term (PT) are reported (excluding Uncoded), along with TEAEs of interest: conjunctivitis (customized MedDRA query defined as PT: conjunctivitis, conjunctivitis bacterial, conjunctivitis viral, conjunctivitis allergic, and atopic keratoconjunctivitis), infections (MedDRA system organ class: Infections and infestations), laboratory abnormalities (TEAE identified in the Investigations MedDRA system organ class), and hypertension (single MedDRA PT).

Statistical analysis

Continuous data are summarized as means and standard deviations or standard errors, categorical data are summarized as counts and percentages. Only observed data are summarized, with no imputation for missing data. Factors contributing to missing data include (1) patients initiating therapy without follow-up visit yet as of this interim data cut off, (2) patients only completing a partial PRO questionnaire which were treated as missing when calculating total scores, and (3) patients missing study visits during COVID. Longitudinal changes from therapy start (whether at or after study entry) to last observation (last available observation before the data cut-off date [July 30, 2021] or treatment discontinuation) were calculated to assess treatment effectiveness. Nominal *P* values were generated for within-treatment group changes from baseline for hypothesis-generating purposes; and no adjustments for multiplicity were performed. Comparisons between treatment groups are descriptive. Kaplan–Meier analysis was used to examine times to discontinuation and Fisher's exact test was used to compare between treatment groups. All other safety data were summarized descriptively.

RESULTS

Baseline characteristics

Of the 1329 children enrolled at the time of this analysis, 241 (78.8%) received just one treatment (dupilumab, 94; methotrexate, 77; cyclosporine, 70). A total of 306 children received ≥1 of the 3 systemic treatments (dupilumab, 144; methotrexate, 114; cyclosporine, 121). Fifty-seven received 2 systemic treatments and 8 received all 3.

At baseline, the mean age of patients in the dupilumab, methotrexate, and cyclosporine treatment groups were 7.8, 7.1, and 7.2 years, respectively, and approximately 50% were males (Table I). Treatments varied by enrollment region, with the most common treatments being dupilumab in North America, methotrexate in Latin America, and cyclosporine in Europe, Middle East, and Africa and Asia-Pacific. Patients who received dupilumab had received more prior therapies than those in the other 2 groups. Though patients who received methotrexate appeared to have slightly less severe disease than those who received dupilumab or cyclosporine (mean EASI 16.8, 19.9, and 18.5; BSA 34.6%, 39.9%, and 40.4%, respectively). Overall, there were no statistically significant differences between treatment groups at baseline in most clinical and patient reported outcomes except for worst itching

Table I. Baseline demographics and disease characteristics

	Dupilumab (*n* = 144)	Methotrexate (*n* = 114)	Cyclosporine (*n* = 121)
Age, years, mean (SD)	7.8 (2.3)	7.1 (2.7)	7.2 (2.7)
Age group, *n* (%)			
<2 y	0	1 (0.9)	2 (1.7)
2 to <6 y	24 (16.7)	33 (28.9)	31 (25.6)
6 to <12 y	120 (83.3)	80 (70.2)	88 (72.7)
Male, *n* (%)	76 (52.8)	68 (59.6)	59 (48.8)
Race, *n/n* (%)			
White	88/132 (66.7)	70/105 (66.7)	70/113 (61.9)
Black or African American	19/132 (14.4)	13/105 (12.4)	10/113 (8.8)
Asian	18/132 (13.6)	10/105 (9.5)	19/113 (16.8)
American Indian or Alaskan Native	1/132 (0.8)	4/105 (3.8)	3/113 (2.7)
Other	6/132 (4.5)	8/105 (7.6)	11/113 (9.7)
Hispanic/Latino	25/119 (21.0)	45/102 (44.1)	38/101 (37.6)
Region, *n* (%)			
EMEA	61 (42.4)	36 (31.6)	53 (43.8)
NA	65 (45.1)	37 (32.5)	18 (14.9)
LATAM	8 (5.6)	39 (34.2)	34 (28.1)
Asia-Pacific	10 (6.9)	2 (1.8)	16 (13.2)
Age at AD onset, y, mean (SD)	1.2 (1.7)	1.5 (1.8)	1.2 (1.6)
Prior therapies, *n* (%)			
Topical corticosteroids	128 (88.9)	79 (69.3)	85 (70.2)
Topical calcineurin inhibitors	64 (44.4)	29 (25.4)	47 (38.8)
Topical antibiotics	27 (18.8)	16 (14.0)	8 (6.6)
Crisaborole	7 (4.9)	3 (2.6)	0
Other nonsystemic therapy	44 (30.6)	17 (14.9)	36 (29.8)
Systemic corticosteroids	15 (10.4)	17 (14.9)	20 (16.5)
Cyclosporine	34 (23.6)	18 (15.8)	—
Methotrexate	19 (13.2)	—	6 (5.0)
Dupilumab	—	3 (2.6)	2 (1.7)
UV therapy	1 (0.7)	4 (3.5)	6 (5.0)
Mycophenolate	5 (3.5)	3 (2.6)	1 (0.8)
Azathioprine	1 (0.7)	1 (0.9)	1 (0.8)
Omalizumab	1 (0.7)	0	1 (0.8)
AD severity scores, mean (SD)			
EASI [0-72*]	19.9 (14.6) (*n* = 143)	16.8 (12.6) (*n* = 113)	18.5 (12.2) (*n* = 119)
BSA, % [0-100*]	39.9 (24.5) (*n* = 137)	34.6 (21.2) (*n* = 110)	40.4 (22.7) (*n* = 111)
Worst itching previous night† [0-10*]	5.4 (2.8)‡ (*n* = 113)	4.1 (3.1) (*n* = 74)	5.2 (3.1)§ (*n* = 82)
Worst itching current day† [0-10*]	3.9 (2.7)‖ (*n* = 112)	2.9 (2.6) (*n* = 74)	3.7 (2.7) (*n* = 82)
Worst scratching/itching last 24 h¶ [0-10*]	6.2 (2.8) (*n* = 19)	7.0 (2.6) (*n* = 29)	6.2 (2.5) (*n* = 28)
POEM [scale 0-28*]	17.8 (7.0) (*n* = 141)	17.6 (7.5) (*n* = 107)	18.1 (6.6) (*n* = 117)
CDLQI#/IDQOL** [scale 0-30*]	13.0 (7.3) (*n* = 141)	11.6 (6.9) (*n* = 107)	11.9 (7.4) (*n* = 117)
DFI [scale 0-30*]	12.4 (7.4) (*n* = 141)	12.3 (7.6) (*n* = 108)	13.1 (7.8) (*n* = 114)

AD, Atopic dermatitis; *BSA*, body surface area; *CDLQI*, Children's Dermatology Life Quality Index; *DFI*, Dermatitis Family Impact; *EASI*, Eczema Area and Severity Index; *EMEA*, Europe, Middle East, and Africa; *IDQOL*, Infants' Dermatitis Quality of Life Index; *LATAM*, Latin America; *NA*, North America; *POEM*, Patient-Oriented Eczema Measure; *SD*, standard deviation.

*Higher scores indicate higher severity.

†Age ≥6 years.

‡$P < .005$ dupilumab vs methotrexate.

§$P < .05$ cyclosporine vs methotrexate.

‖$P < .05$ dupilumab vs methotrexate.

¶Age <6 years.

#Age ≥4 years.

**Age <4 years.

(previous night) and worst itching (current day) for children <6 years old. Patients who initiated dupilumab or cyclosporine had higher itch intensity compared to patients who initiated methotrexate.

Treatment durations and doses

Median treatment durations were 8.1, 13.0, and 10.7 months for dupilumab, methotrexate, and cyclosporine, respectively. Median doses were as follows: dupilumab 300 mg every 4 weeks (q4w; 15-30 kg, n = 76), 250 mg q4w (children 2−<6 years weighing 5-15 kg, n = 2), 200 mg every 2 weeks (q2w; 30-60 kg n = 53), or 300 mg q2w (≥60 kg, n = 3); methotrexate 8.8 mg/kg/week (n = 107); and cyclosporine 3.7 mg/kg/day (n = 113). At the time of last assessment, 91.7% of dupilumab patients, 71.1% of methotrexate patients, and 57.0% of cyclosporine patients were still taking their respective medications.

Outcomes

Patients who received dupilumab had the largest improvement in mean EASI score from treatment start (−12.4; $P < .001$), followed by methotrexate (−5.7; $P < .001$), then cyclosporine (−3.3; $P = .086$) (Fig 1). Improvements in mean affected BSA followed a similar pattern: dupilumab (−19.9%; $P < .001$), methotrexate (−11.8%; $P < .001$), and cyclosporine (−8.8%; $P = .009$).

Children aged ≥6 years who received dupilumab had significant improvements in mean night-time (−2.1; $P < .001$) and daytime (−1.5; $P = .005$) itching, but no significant benefits were seen with methotrexate or cyclosporine (Fig 2). Children aged <6 years obtained significant reductions in scratching/itching with dupilumab (−3.6; $P = .011$) and methotrexate (−1.4; $P = .020$), but not cyclosporine.

The largest improvement in mean POEM scores was observed among patients who received dupilumab (−7.0; $P < .001$), followed by methotrexate (−4.7; $P < .001$), then cyclosporine (−1.5; $P = .33$) (Fig 3). Improvements in mean CDLQI/IDQOL were similar with dupilumab (−4.3; $P < .001$) and methotrexate (−3.6; $P < .001$), while cyclosporine had no significant impact (−0.5; $P = .91$). Mean DFI improvements were also similar with dupilumab (−3.6; $P < .001$) and methotrexate (−4.0; $P < .001$), while cyclosporine had little impact (−1.4; $P = .30$).

Treatment persistence

The treatment discontinuation rate was lower for dupilumab (8.3%) than methotrexate (28.9%; $P < .0001$) and cyclosporine (43.0%; $P < .0001$) (Supplementary Table I, available via Mendeley at https://dx.doi.org/10.17632/trtrtn39sn.1). Time to discontinuation was longest for dupilumab, then methotrexate, then cyclosporine (Fig 4). Patients were less likely to discontinue dupilumab due to lack of efficacy (1.4% vs 5.3% for methotrexate and 9.1% for cyclosporine), disease well-controlled (0% vs 7.0% and 6.6%), caregiver/patient decision (0% vs 4.4% and 5.8%), and adverse events (AEs) (1.4% vs 1.8% and 5.0%) (Supplementary Table I, available via Mendeley at https://dx.doi.org/10.17632/trtrtn39sn.1).

Safety

Fewer patients receiving dupilumab had ≥1 TEAE than those receiving methotrexate or cyclosporine (18.1% vs 29.8% and 31.4%) and there were low rates of severe TEAEs (0 vs 1.8% and 2.5%), serious TEAEs (1.4% vs 1.8% and 1.7%), and TEAEs leading to withdrawal from the study (0 vs 0.9% and 1.7%) (Supplementary Table II, available via Mendeley at https://dx.doi.org/10.17632/trtrtn39sn.1). The 2 most common TEAEs were different in each treatment group: allergic conjunctivitis (2.1%) and conjunctivitis (2.1%) for dupilumab; AD (7.0%), abdominal pain and molluscum contagiosum (both 3.5%) for methotrexate; and AD (9.9%) and impetigo (3.3%) for cyclosporine (Supplementary Table III, available via Mendeley at https://dx.doi.org/10.17632/trtrtn39sn.1).

Regarding TEAEs of interest (Supplementary Table IV, available via Mendeley at https://dx.doi.org/10.17632/trtrtn39sn.1), conjunctivitis was most common with dupilumab, but fewer patients receiving dupilumab had "Infections and infestations" than those receiving methotrexate or cyclosporine (9.0% vs 14.9% and 13.2%). There was only one laboratory abnormality (cyclosporine) and no hypertension.

DISCUSSION

In this 2-year interim analysis, we examined outcomes among patients aged <12 years with moderate-to-severe AD who received dupilumab, methotrexate, and cyclosporine as a systemic treatment. Sample sizes for other systemic therapies taken by patients enrolled in PEDISTAD were not sufficiently sized for analysis at the time of this interim data analysis. Future publications will include other systemic therapy groups as more patient data become available.

Significant improvements in all 8 reported outcomes (EASI, BSA, night and day itching, scratching/itching, POEM, CDLQI/IDQOL, and DFI) were observed among patients who received dupilumab. Significant improvements in 6/8 outcomes (all except night and day itching) were observed with

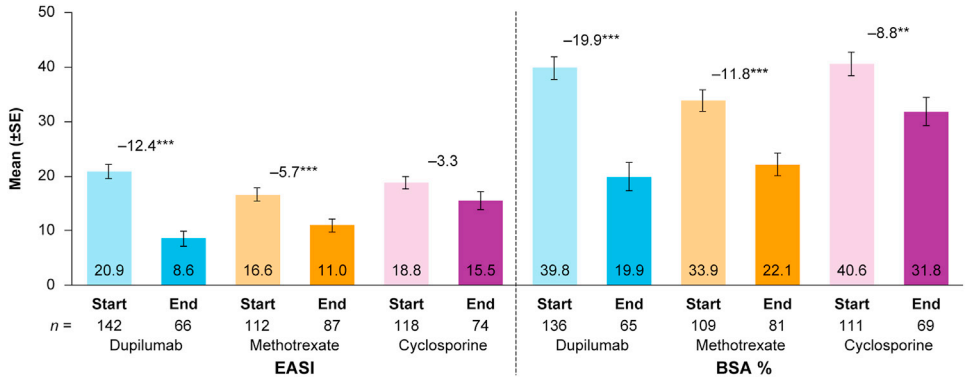

Fig 1. Mean percent affected BSA and EASI scores for AD at the start of treatment ("Start") and the last observation ("End") in the 3 systemic treatment groups of interest. *BSA*, Body surface area; *EASI*, Eczema Area and Severity Index; *SE*, standard error. Changes may not equal the difference between Start and End due to rounding. $^{**}P < .01$; $^{***}P < .001$.

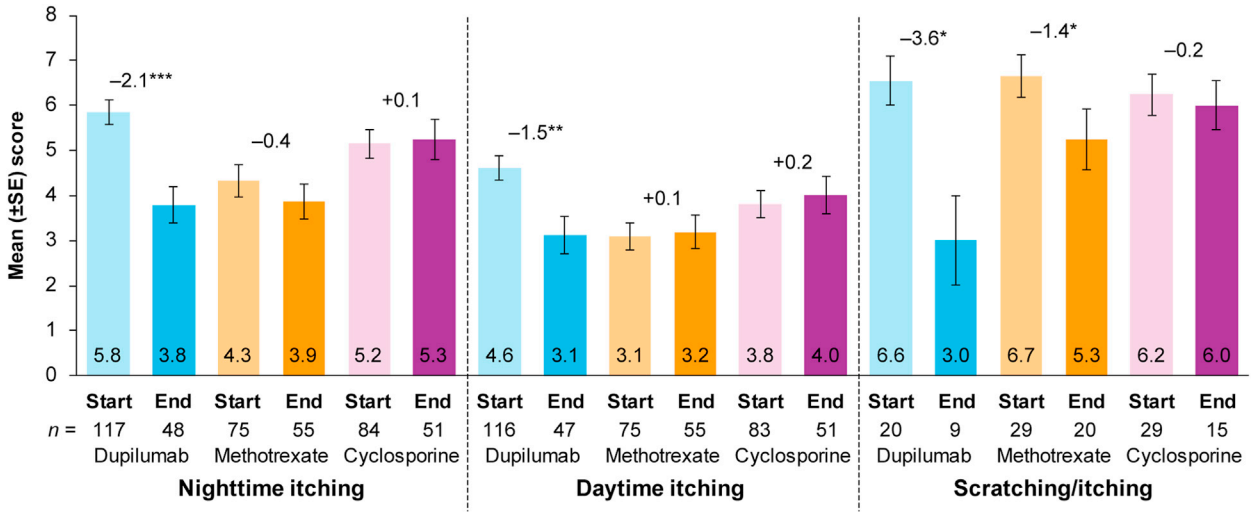

Fig 2. Mean worst itching (previous night and current day; age ≥6 years) and worst scratching/itching (previous 24 hours; age <6 years) at the start of treatment ("Start") and the last observation ("End") in the 3 systemic treatment groups of interest. *SE*, Standard error. Changes may not equal the difference between Start and End due to rounding. $^{*}P < .05$; $^{**}P < .01$; $^{***}P < .001$.

methotrexate. Somewhat surprisingly, cyclosporine was associated with a significant improvement in only 1/8 outcomes (BSA). This may be due to difficulties adhering to a twice daily schedule or issues with tolerability.

The baseline disease characteristics of the children included in the current analysis reflect a multidimensional AD disease burden despite standard treatment. However, the high burden and relatively low proportion (23.0%) of children receiving one of the 3 systemic therapies in this real-world study suggests an unmet need for effective therapies with demonstrated safety for children with moderate-to-severe AD. Low use of these systemic therapies may be due to concerns about AEs with immunosuppressants and the unavailability of newer agents (eg dupilumab) in many countries at the time of the data cut.

To put our results into context, the mean EASI score among children who received dupilumab improved from 20.9 to 8.6, close to mild AD.[12] In the methotrexate and cyclosporine groups, mean EASI scores improved, but remained well within the moderate band.[12]

Mean POEM scores for patients in each systemic treatment group improved from severe (17-24) to

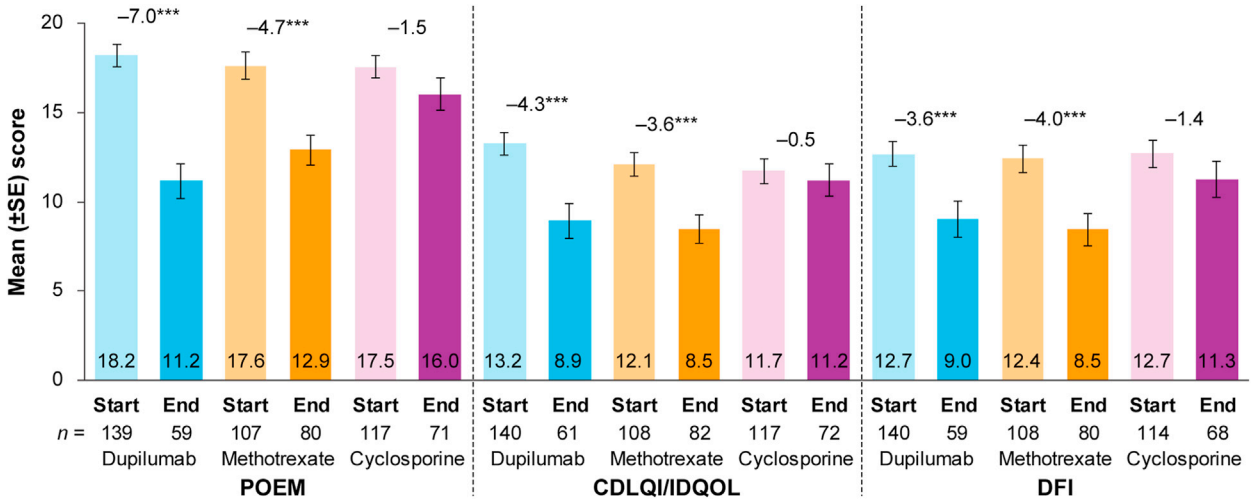

Fig 3. Mean POEM, combined CDLQI/IDQOL, and DFI scores at the start of treatment ("Start") and the last observation ("End") in the 3 systemic treatment groups of interest. *CDLQI*, Children's Dermatology Life Quality Index; *DFI*, Dermatitis Family Impact; *IDQOL*, Infants' Dermatitis Quality of Life; *POEM*, Patient-Oriented Eczema Measure; *SE*, standard error. Changes may not equal the difference between Start and End due to rounding. ***$P < .001$.

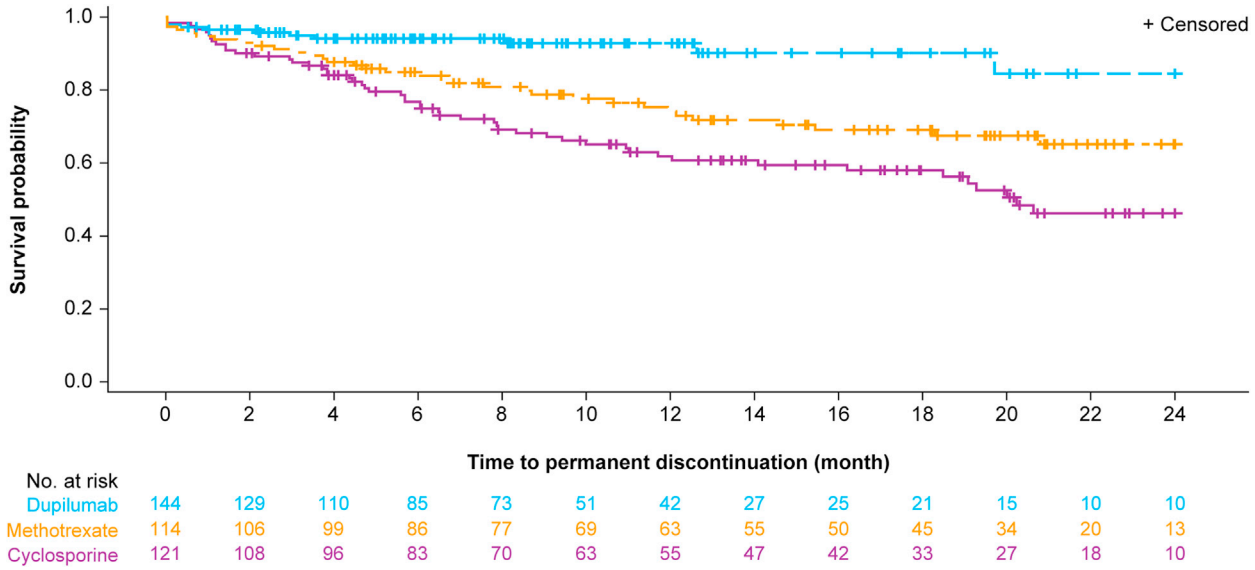

Fig 4. Treatment discontinuations in the 3 systemic therapy groups.

moderate (8-16), on average,[13] with the largest improvement among those who received dupilumab. Mean DFI scores improved from AD having a moderate (11-20) to a low impact (6-10), on average, on family life according to suggested bandings[14] in the dupilumab and methotrexate groups but remaining moderate, on average, in the cyclosporine group.

We found much lower treatment discontinuation rates for dupilumab than methotrexate and cyclosporine, which likely indicates better treatment satisfaction. Some patients discontinued methotrexate or cyclosporine due to having well-controlled disease, but none discontinued dupilumab for this reason. This could indicate that dupilumab is seen as a long-term treatment due to its acceptable safety profile, while methotrexate and cyclosporine tend to be discontinued once control has been achieved. Indeed, higher rates of cyclosporine discontinuation may be expected as cyclosporine is frequently prescribed as a short-term rescue medication that is intended to be discontinued. Lower overall discontinuation rates for dupilumab than methotrexate or cyclosporine (9% vs 59% vs 63%, respectively) have been previously reported

after 1 year among adults in the BioDay registry.[15] In that study, approximately half of the methotrexate and cyclosporine patients discontinued treatment due to ineffectiveness and/or side effects.[15] Additionally, lower discontinuation rates for dupilumab than cyclosporine (18% vs 89%) were reported among adults at 16 months.[16] Reasons for stopping dupilumab in that study included persistent clinical remission (7.4%), primary inefficacy (4.7%), and cutaneous AEs (2.0%); and for cyclosporine, AEs (23.5%), persistent clinical remission (15.6%), and minimal/absent improvement (11.7%).[16] Similarly, Napolitano et al[17] reported lower discontinuation rates with dupilumab than cyclosporine (14.0% vs 78.9%) among adults at 72 weeks, with 42% stopping cyclosporine due to AEs.

In the current study, a lower percentage of patients who received dupilumab reported ≥1 TEAE compared to those who received methotrexate or cyclosporine and they were less likely to withdraw from the study due to TEAEs. Overall, the safety of dupilumab was consistent with its known safety profile.[8,9]

Although the numbers were small in all groups and significance was not tested, a lower proportion of patients who received dupilumab had skin infections (eg impetigo or molluscum contagiosum) than those who received methotrexate or cyclosporine. This observation supports data from RCTs that have shown reduced rates of nonherpetic skin infections among patients treated with dupilumab versus placebo,[18-21] as has a real-world study that compared skin infections before and after initiating dupilumab.[22] In the current study, a lower percentage of patients who received dupilumab had any "infections and infestations" than those who received methotrexate or cyclosporine, mainly due to fewer skin infections. However, conjunctivitis was more common with dupilumab than methotrexate or cyclosporine. Conjunctivitis is a common comorbidity in patients with AD[23] and a labeled adverse reaction described in the product information.[4] Other TEAEs of interest were rare.

Since this study was not a RCT, limitations included unblinded treatment groups, no fixed dosage regimens, inconsistent dose reporting across countries, and varying treatment durations. Additionally, the analysis employed in this manuscript reflects patterns of use and is not intended to suggest superiority of any specific treatment groups. Treatments and treatment durations also varied by region, likely because of differences in dupilumab approval and availability. Only 306/1329 children (23.0%) received dupilumab, methotrexate, and/or cyclosporine, possibly due to a lack of availability in some countries and/or reluctance to take systemic medication. Also, median treatment durations were relatively low for a 2-year analysis, most likely because patients had not been enrolled of the full 2 years and could initiate new treatments at any time during the study.

In conclusion, dupilumab treatment in patients aged <12 years with inadequately controlled moderate-to-severe AD enrolled in PEDSITAD was associated with numerically greater improvements in AD severity, better treatment adherence/persistence, and a lower incidence of TEAEs than methotrexate or cyclosporine in this 2-year interim analysis.

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Conflicts of interest

Dr Paller has been an investigator, consultant, and/or data and safety monitoring board member for AbbVie, Abeona Therapeutics, Amryt Pharma, Azitra, BioCryst, BMS, Boehringer Ingelheim, Castle Creek Biosciences, Catawba Research, Dermavant, Eli Lilly, Galderma, InMed Pharmaceuticals, Incyte, Janssen, Krystal Biotech, LEO Pharma, Novartis, Regeneron Pharmaceuticals Inc, Sanofi, Seanergy, TWi Biotechnology, and UCB. Dr de Bruin-Weller has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Amgen, Eli Lilly, Galderma, Janssen, LEO Pharma, Pfizer, Regeneron Pharmaceuticals Inc, and Sanofi Genzyme. Dr Marcoux has been an investigator for AbbVie, Amgen, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, and Regeneron Pharmaceuticals Inc. They have served as a consultant for AbbVie, Amgen, BMS, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, and UCB, and is or has been a speaker for AbbVie, Amgen, BMS, Novartis, Pfizer, Regeneron Pharmaceuticals Inc, and Sanofi Genzyme. Dr Baselga has been an investigator for AbbVie, Boehringer Ingelheim, Dermira, Eli Lilly, LEO Pharma, Pfizer, and Novartis, and served as a consultant for Almirall, Galderma, Novartis, Pfizer, Pierre-Fabre, Regeneron Pharmaceuticals Inc, and Sanofi Genzyme. Dr Carvalho has been a speaker for Expanscience, Galderma, Johnson & Johnson Consumer Health, Mantecorp Skincare, Megalabs, and Royal Canin. They have been a consultant for Johnson & Johnson and have been an investigator for Sanofi. Dr Ardusso has been a consultant and/or advisory board member, and/or speaker for AstraZeneca, GSK, and Sanofi and has been an investigator for Novartis, Sanofi Genzyme, Amgen, Chiesi, AstraZeneca, Areteria, bellus, and Upstream Bio. Dr Pasmans has been a consultant, advisory board member, and or speaker for LEO Pharma, Pfizer, Regeneron, and Sanofi Genzyme. They have been an advisory board member, and or speaker or investigator for LEO Pharma, Regeneron Pharmaceuticals, Sanofi

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JAAD Game changer

JAAD Game Changer: Lymphomatoid papulosis: Treatment response and associated lymphomas in a study of 180 patients

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How did this article change the practice of dermatology?

- Lymphomatoid papulosis is a relatively rare $CD30^+$ lymphoproliferative disorder that has a relatively lackluster clinical presentation and course. Due to its infrequency, providing patients with proper counseling, screening, and long-term expectations can be difficult.
- From one of the largest cohorts of LyP-affected patients studied, investigators were able to provide some risk factors for developing lymphoma, treatment expectations, and guidance for long-term surveillance.
- These findings have certainly helped me follow and manage my handful of LyP-afflicted patients.

Conflicts of interest: None disclosed.

Note: A Game Changer is a short narrative stating how an article that originally appeared in *JAAD* changed the game of dermatology. The Game Changer author is not the author of the original article.

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