Disease characteristics, comorbidities, treatment patterns and quality of life impact in children <12 years old with atopic dermatitis

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Research letter

Disease characteristics, comorbidities, treatment patterns and quality of life impact in children <12 years old with atopic dermatitis: Interim results from the PEDISTAD Real-World Registry

To the Editor: To address the issue of limited real-world long-term data in children with atopic dermatitis (AD), we designed the PEDISTAD observational study (NCT03687359). This ongoing, international, longitudinal, 5-year registry assesses the disease course, comorbidities, treatment, and disease burden in children with moderate-to-severe AD.[1] Here, we present baseline interim data.

The study design and inclusion/exclusion criteria for PEDISTAD have been reported.[1] Briefly, PEDISTAD included children aged <12 years at baseline with investigator-assessed moderate-to-severe disease receiving systemic medications for AD (including biologics, cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, and corticosteroids), phototherapy, or topical treatment (but otherwise candidates for systemic therapy).

Between September 2018 and July 2020, 732 children were enrolled at 106 sites in North America (38.4%), Latin America (23.0%), Europe, the Middle East and Africa (30.3%), and Asia-Pacific (8.3%). As shown in Table I, 61.2% of children had ≥1 selected comorbidity at baseline, mainly atopic comorbidities (59.0%). Most (77.2%) were receiving nonsystemic medications for AD at baseline, while 23.1% were receiving systemic medications for AD (Table I).

Mean (SD) body surface area affected by AD was 33.3% (21.0%), Eczema Area and Severity score was 14.4 (10.7), and Patient-Oriented Eczema Measure score was 15.6 (7.2) (Table I) —both consistent with moderate disease —with a high proportion of children suffering daily from dry/rough, itchy, cracked, flaking skin, and affected sleep (Fig 1). Self-reported mean worst itch score during the previous night was 4.9 (2.9) among children aged 6 to younger than 12 years, with slightly higher worst scratching scores in younger children (0-<6 years) (Table I). The mean Infant's Dermatitis Quality of Life scores of children aged 0 to 3 years was 10.3 (6.1). Those aged 4 to younger than 12 years reported a mean Children's Dermatology Life Quality Index of 10.8 (6.7) (moderate) (Table I). The overall mean Dermatitis Family Impact score was 10.9 (7.4) (Table I).

Overall, these interim baseline data from PEDISTAD show a significant disease burden characterized by itch and impact on sleep, quality of life, and family, demonstrating a substantial impact of AD on children and their caregivers. This could be due to the low use of systemic therapies (<25%), possibly related to the limited treatment options and concerns about adverse effects with long-term immunosuppressant use.

Most of the children in PEDISTAD had concomitant atopic comorbidities, which is consistent with previous studies that found an increased prevalence of comorbid asthma, allergic rhinitis, and food allergy among children with moderate-to-severe AD.[2,3]

The median age of disease onset in this PEDISTAD cohort was 8 months. AD is commonly diagnosed before age 5 years and often persists into adulthood.[4] People with an early onset of AD have a distinct disease progression and an increased risk of developing other atopic comorbidities.[5] Early-onset AD can therefore have a significant impact on the lives of children and their family for long periods of time.

The main limitation of this observational study is the low patient numbers in the youngest age group.

In summary, we found a high disease and family burden among children younger than 12 years old with moderate-to-severe AD and with inadequately controlled disease at baseline. There remains a need for effective and safe therapies for long-term disease control in this pediatric population. For a video abstract of this article, see Video 1 (available via Mendeley at https://doi.org/10.17632/kcr4hndftx.1).

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Table I. Baseline demographics and clinical characteristics

Baseline characteristics	0 to <2 years (n = 77)	2 to <6 years (n = 224)	6 to <12 years (n = 431)	Total (N = 732)
Age, y, mean (SD)	1.12 (0.50)	3.58 (1.09)	8.50 (1.74)	6.22 (3.18)
Sex, male, n (%)	49 (63.6)	125 (55.8)	208 (48.3)	382 (52.2)
Race, n/N1 (%)				
White	56/77 (72.7)	139/214 (65.0)	264/413 (63.9)	459/704 (65.2)
Black or African American	8/77 (10.4)	24/214 (11.2)	58/413 (14.0)	90/704 (12.8)
Asian	6/77 (7.8)	27/214 (12.6)	59/413 (14.3)	92/704 (13.1)
Multiple or other	7/77 (9.1)	24/214 (11.2)	32/413 (7.7)	63/704 (8.9)
Any concomitant AD comorbidity, n (%)	24 (31.2)	131 (58.5)	293 (68.0)	448 (61.2)
Type 2 comorbidity	24 (31.2)	130 (58.0)	278 (64.5)	432 (59.0)
Allergic rhinitis	4 (5.2)	49 (21.9)	198 (45.9)	251 (34.3)
Asthma	1 (1.3)	51 (22.8)	153 (35.5)	205 (28.0)
Food allergy	22 (28.6)	82 (36.6)	138 (32.0)	242 (33.1)
Allergic conjunctivitis	0	13 (5.8)	80 (18.6)	93 (12.7)
Eosinophilic esophagitis	0	1 (0.4)	6 (1.4)	7 (1.0)
Nasal polyposis	0	0	6 (1.4)	6 (0.8)
Anxiety*	0	5 (2.2)	32 (7.4)	37 (5.1)
ADD/ADHD	0	1 (0.4)	30 (7.0)	31 (4.2)
Age at AD onset, y, median (IQR)	0.3 (0.2-0.5)	0.5 (0.3-1.0)	1.0 (0.3-4.0)	0.7 (0.3-2.0)
Nonsystemic medications for AD†	57 (74.0)	171 (76.3)	337 (78.2)	565 (77.2)
Topical antibiotics	3 (3.9)	18 (8.0)	40 (9.3)	61 (8.3)
TCS	52 (67.5)	154 (68.8)	306 (71.0)	512 (69.9)
TCI	11 (14.3)	56 (25.0)	121 (28.1)	188 (25.7)
Crisaborole	1 (1.3)	12 (5.4)	17 (3.9)	30 (4.1)
Systemic medications for AD‡	9 (11.7)	50 (22.3)	110 (25.5)	169 (23.1)
Cyclosporine	0	16 (7.1)	43 (10.0)	59 (8.1)
Methotrexate	0	21 (9.4)	45 (10.4)	66 (9.0)
Dupilumab	0	5 (2.2)§	14 (3.2)	19 (2.6)
Azathioprine	0	1 (0.4)	1 (0.2)	2 (0.3)
Mycophenolate mofetil	0	1 (0.4)	4 (0.9)	5 (0.7)
Systemic corticosteroids	9 (11.7)	17 (7.6)	12 (2.8)	38 (5.2)
Phototherapy	2 (2.6)	5 (2.2)	21 (4.9)	28 (3.8)
EASI, mean (SD) [0-72]¶	15.1 (10.3)	13.2 (9.3)	15.0 (11.3)	14.4 (10.7)
BSA % affected by AD, mean (SD) [0-100%]¶	36.4 (20.6)	31.7 (20.8)	33.6 (21.1)	33.3 (21.0)
POEM, mean (SD) [0-28]¶	15.7 (6.6)	16.1 (7.5)	15.3 (7.2)	15.6 (7.2)
CDLQI, mean (SD) [0-30]¶	N/A	10.8 (6.0)‖	10.8 (6.9)	10.8 (6.7)
IDQOL, mean (SD) [0-30]¶	10.3 (6.1)**		N/A	N/A
Caregiver-assessed worst scratching during the previous 24 hours, NRS, mean (SD) [0-10]¶	6.0 (2.6)	5.9 (2.8)	N/A	5.9 (2.7)
Child-reported worst itching during the previous night, peak pruritus NRS, mean (SD) [0−10]¶	N/A	N/A	4.9 (2.9)	N/A
Child-reported worst itching during the current day, peak pruritus NRS, mean (SD) [0-10]¶	N/A	N/A	3.8 (2.7)	N/A
DFI, mean (SD) [0-30]¶	11.1 (7.0)	12.0 (7.9)	10.3 (7.1)	10.9 (7.4)

AD, atopic dermatitis; *ADD*, attention deficit disorder; *ADHD*, attention deficit-hyperactivity disorders; *BSA*, body surface area; *CDLQI*, Children's Dermatology Life Quality Index; *DFI*, Dermatitis Family Impact; *EASI*, Eczema Area and Severity Index; *IDQOL*, Infants' Dermatitis Quality of Life Index; *IQR*, interquartile range; *N/A*, not available; *NRS*, Numerical Rating Scale; *POEM*, Patient-Oriented Eczema Measure; *SD*, standard deviation; *TCS*, topical corticosteroids; *TCI*, topical calcineurin inhibitors.

N1 used to calculate the percentage of race is smaller than N (=732) due to missing values.

*Anxiety was collected through the combination of patient reported and medical records.

†Only key nonsystemic AD medications are listed. Some children were on other nonsystemic treatments; eg, coal tar, chlorine.

‡Only key systemic AD medications are listed. Some children were on other systemic medications; eg, antibiotics, antihistamines/antiallergics, folic acid.

§Off-label treatment in children aged <6 years old.

¶Score ranges; low scores indicate good quality of life and better disease control in each case.

‖Assessed in children aged 4 to <6 years old (N1 = 117).

**Assessed in children aged ≤3 years (N1 = 184).

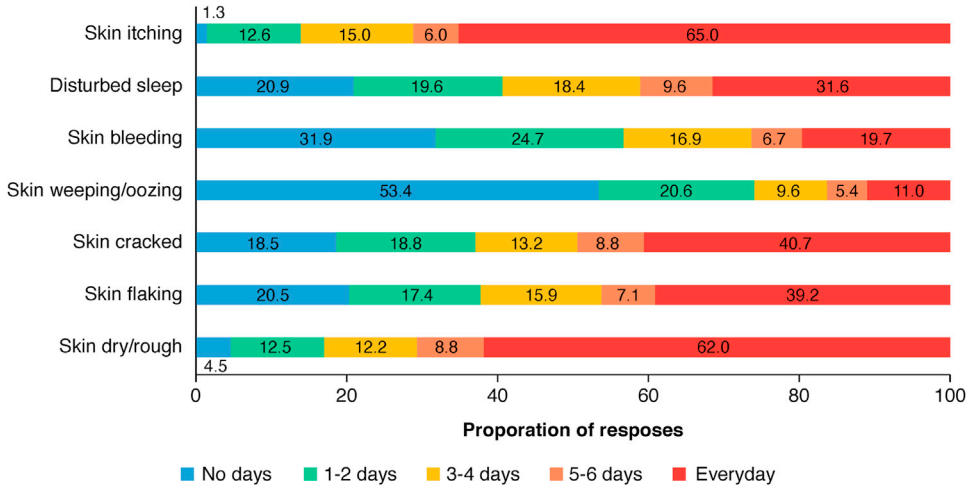

Fig 1. Atopic dermatitis. Proportions of children with each response on the POEM questionnaire (all age groups). The number of days are provided for the previous week. *POEM*, Patient-Oriented Eczema Measure.

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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 PEDISTAD.

Keywords: atopic dermatitis; children; disease burden; family impact; quality of life; real-world.

Reprints not available from the authors.

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Conflicts of interest

Dr Paller has been an investigator for AbbVie, AnaptysBio, BMS, Eli Lilly, Galderma, Incyte, LEO Pharma, Janssen, Novartis, Regeneron Pharmaceuticals, Inc, Sanofi; and a consultant for AbbVie, Abeona, Almirall, Asana Biosciences, Boehringer Ingelheim, BridgeBio Pharma, Dermavant, Dermira, Eli Lilly, Exicure, Forte, Galderma, Incyte, InMed Pharmaceuticals, Janssen, LEO Pharma, Lifemax, Novartis, Pfizer, Rapt Therapeutics, Regeneron, Sanofi Genzyme, Sol Gel, UCB. Dr Guttman-Yassky has been investigator for AbbVie, BMS, Eli Lilly, Galderma, Glenmark, GlaxoSmithKline, LEO Pharma, Pfizer, Regeneron Pharmaceuticals, Inc, Sanofi; a consultant for AbbVie, Anacor, Asana Biosciences, Daiichi Sankyo, DBV, Dermira, Eli Lilly, Galderma, Glenmark, GlaxoSmithKline, Kiniksa Pharmaceuticals, Kyowa, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Realm, Regeneron Pharmaceuticals, Inc, Sanofi; received research grants from AbbVie, BMS, Dermira, Galderma, Innovaderm, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc, Sanofi. Dr Schuttelaar has been an advisory board member for Eli Lilly, LEO Pharma, Pfizer, Sanofi Genzyme; an investigator for AbbVie, Novartis, Regeneron Pharmaceuticals, Inc, Sanofi Genzyme; a consultant for Regeneron Pharmaceuticals, Inc; and has received research grants from Novartis, Sanofi Genzyme. Dr Irvine has received honoraria for

consultancy from AbbVie, Arena Pharmaceuticals, BenevolentAI, Chugai, Dermavant, Eli Lilly, Genentech, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sanofi, UCB. Dr Baselga has been an investigator for AbbVie, Boehringer Ingelheim, Dermira, Eli Lilly, LEO Pharma, Pfizer, Novartis; and a consultant for Almirall, Galderma, Novartis, Pfizer, Pierre-Fabre, Regeneron Pharmaceuticals, Inc, Sanofi Genzyme. Dr Kataoka has received honoraria for lectures and research grants from Sanofi; and research grants from AbbVie, Eli Lilly, LEO Pharma, Maruho, Pfizer, Otsuka. Dr Antila has participated in clinical studies funded by AbbVie, AstraZeneca, EMS, Eurofarma, GlaxoSmithKline, Humanigen, Janssen, Novartis, Sanofi Genzyme; and participated in conferences and consultancy activities for Aché, AstraZeneca, Chiesi, Eurofarma, IPI ASAC Brasil, Sanofi. Dr de Bruin-Weller has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Eli Lilly, Galderma, Janssen, LEO Pharma, Pfizer, Regeneron Pharmaceuticals, Inc, Sanofi Genzyme, UCB. Dr Marcoux has been investigator for AbbVie, Amgen, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer; a consultant for AbbVie, Amgen, BMS, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc, Sanofi Genzyme, UCB; and a speaker for AbbVie, Amgen, BMS, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc, Sanofi Genzyme. Dr Abramova was an employee of Regeneron Pharmaceuticals, Inc when the study was conducted and may hold stock and/or stock options in the company. Dr Rizova was an employee of Sanofi Genzyme when the study was conducted and may hold stock and/or stock options in the company. Mr Liu is an employee of Tigermed-BDM Inc. and is working as a consultant with Sanofi. Dr Zhang is an employee of Sanofi Genzyme and may hold stock and/or stock options in the company.

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