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Efficacy of ixekizumab on nail psoriasis in paediatric patients with moderate-to-severe psoriasis: a post hoc analysis from IXORA-PEDS

Dear Editor,

Nail psoriasis (NP) has been proposed as a potential clinical predictor for a more severe disease course in children with psoriasis, but data regarding NP in children are scarce.[1–3] Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin(IL)-17A, is an EMA and FDA approved treatment for paediatric (≥6 years old) and adult patients with moderate-to-severe psoriasis and provides rapid clinically meaningful improvements in skin, itch and quality of life (QoL) outcomes at week 12.[3,4] In IXORA-PEDS, a phase III multicentre, double-blind, randomized, placebo-controlled study (NCT03073200), which assessed efficacy and safety of IXE in paediatric patients with moderate-to-severe psoriasis,[3] 50% of patients randomized to IXE at baseline achieved complete clearance (Nail Psoriasis Severity Index [NAPSI] score = 0) in their NP by week 48.[4] This *post hoc* analysis provides an in-depth analysis of NP in paediatric psoriasis patients from IXORA-PEDS randomly assigned to IXE through week 48. Overall NP severity, nail bed and nail matrix features at baseline, as well as improvements and clearance of NP over time were evaluated.

Patients were stratified based on fingernail involvement (fingernail NAPSI range: 0–80) as having any degree of NP ('baseline NP', $N = 34$), defined as fingernail NAPSI ≥1, and from that, the subgroup of patients with moderate-to-severe NP ('significant baseline NP', $n = 20/34$) defined as fingernail NAPSI ≥16 and ≥4 fingernails involved.[5]

Consistent with previously published studies,[2,6] in IXORA-PEDS, patients with NP were mostly male and had more severe skin disease, including involvement of other difficult-to-treat areas such as palmoplantar and scalp psoriasis (Table 1). Of note, only one patient with significant baseline NP had concomitant psoriatic arthritis. The average percentage improvements in NAPSI score from baseline were comparable in IXE-treated paediatric patients across cohorts, exhibiting an initial rapid change from baseline up to week 24, with further improvements until week 48 (Fig. 1a). These effects were driven by reductions in both nail matrix and nail bed individual scores, with nail matrix changes primarily affecting the nail plate exhibiting a somewhat slower response (Fig. 1b).

Complete clearance in NP, arguably the most important NP treatment goal from both a patient and clinician perspective,[7] was observed in 17.6% ($n = 6/34$) and 15.0% ($n = 3/20$) of patients with baseline NP and significant baseline NP, respectively, at week 12 (Fig. 1c). Similar to IXE's dynamics of nail clearance in adults,[5] at week 24, the number of patients achieving NAPSI = 0 rapidly increased (50.0%, $n = 17/34$ vs. 40.0%, $n = 8/20$) and plateaued through week 48 (50.0%, $n = 17/34$ vs. 50.0%, $n = 10/20$) in both cohorts.

Limitations of this *post hoc* analysis were the lack of a comparator arm and a low sample size, which prevented the evaluation of NP' impact on young patients' QoL.

In adults, through both direct and indirect comparisons, IXE has demonstrated rapid and/or long-term efficacy in NP[5,8,9] and ranked best among investigated biologics in terms of improvement in nail scores and complete clearance for NP at weeks 24–26, respectively.[7,10] Consistent with the data from adult studies, half of paediatric patients upon treatment with IXE achieved complete clearance in their NP irrespective of disease severity at baseline, confirming and extending the efficacy of IXE in NP to the paediatric population. Furthermore, these results demonstrate the efficacy of IXE in improving both nail matrix and nail bed psoriasis.

Overall, the results of this analysis corroborate the demonstrated efficacy of IXE in NP observed in adults[8,10] and provide new information to physicians who treat paediatric patients with this burdensome and debilitating disease.

Conflict of interest

M.M.B.S received grants from/was involved in clinical trials from Abbvie, Amgen, Celgene, Eli Lilly, Janssen, Leo Pharma and Pfizer. She served as a consultant for Abbvie, Eli Lilly, Janssen, Leo Pharma, Novartis, UCB and Pfizer; fees were paid

Table 1 Baseline characteristics for paediatric patients without baseline nail psoriasis (NP), those with baseline NP (NAPSI ≥1) and the subgroup of patients with baseline NP that had significant baseline fingernail psoriasis (NAPSI ≥16 and ≥4 fingernails involved)

	Patients without baseline NP *N* = 81 NAPSI = 0	Patients with baseline NP *N* = 34 NAPSI ≥1	Subgroup of patients with significant baseline NP† *n* = 20/34 NAPSI ≥16 and ≥4 fingernails
Age (years), mean ± SD	13.9 ± 3.0	13.2 ± 3.5	12.8 ± 3.8
Male sex	33 (40.7)	19 (55.9)	15 (75.0)
White race	69 (86.3)	26 (76.5)	17 (85.0)
BMI (kg/m^2), mean ± SD	23.2 ± 5.8	26.3 ± 8.4	24.9 ± 7.2
Duration of psoriasis since diagnosis (years), mean ± SD	5.8 ± 3.6	5.2 ± 2.9	4.6 ± 3.0
Prior psoriasis treatment			
Non-biologic systemic	24 (29.6)	15 (44.1)	9 (45.0)
Biologic	4 (4.9)	1 (2.9)	0 (0.0)
Phototherapy	15 (18.5)	10 (29.4)	6 (30.0)
Involved BSA (%), mean ± SD	26.6 ± 16.7	28.4 ± 22.6	25.1 ± 21.6
sPGA score, mean ± SD	3.4 ± 0.6	3.9 ± 0.6	3.9 ± 0.6
sPGA = 3	48 (59.3)	9 (26.5)	5 (25.0)
sPGA = 4	31 (38.3)	20 (58.8)	12 (60.0)
sPGA = 5	2 (2.5)	5 (14.7)	3 (15.0)
PASI, mean ± SD	18.9 ± 6.6	21.7 ± 9.2	21.2 ± 8.4
NAPSI (0–80), mean ± SD	–	33.9 ± 29.5	52.0 ± 25.8
NAPSI matrix score† (0–40), mean ± SD	–	18.8 ± 11.3	24.4 ± 9.3
NAPSI bed score† (0–40), mean ± SD	–	15.7 ± 11.4	17.8 ± 11.3
PSSI, mean ± SD	24.7 ± 16.5	33.2 ± 17.1	36.3 ± 17.5
PPASI, mean ± SD	3.9 ± 4.6	10.4 ± 9.5	11.6 ± 10.0
DLQI, mean ± SD	9.6 ± 5.2	8.4 ± 4.2	8.0 ± 3.9
Concomitant PsA	0 (0.0)	1 (2.9)	1 (5.0)

Unless otherwise specified, data are presented as *n* (%).
BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; IXE, ixekizumab; NAPSI, Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; PPASI, Palmoplantar Psoriasis Area and Severity Index; PsA; Psoriatic arthritis, PSSI, Psoriasis Scalp Severity Index; sPGA, static Physician's Global Assessment.
†Patients with significant baseline NP are included in the cohort of patients with baseline NP. ‡Fingernails were divided into quadrants, nail matrix assessed by examining features of pitting, leukonychia, red spots in the lunula or crumbling, with a score of 0 for none, and a maximum score of 4, for features in all nail quadrants. §Fingernails were evaluated for nail bed features of onycholysis, splinter haemorrhages, subungual hyperkeratosis and oil drop (salmon patch) dyschromia in the same manner as nail matrix features.

directly to the institution. A.R has worked as a consultant or speaker for AbbVie, Bausch Health, Bioderma, Celgene, Chema Elektromet, Eli Lilly, Galderma, Janssen, Leo Pharma, Medac, Menlo Therapeutics, Novartis, Pierre-Fabre, Sandoz and Trevi and participated as principal investigator or sub-investigator in clinical trials sponsored by AbbVie, AnaptysBio, Argenx, CellTrion, Drug Delivery Solutions Ltd, Galderma, Genentech, InflaRx, Janssen, Kymab Limited, Leo Pharma, Menlo Therapeutics, MetrioPharm, MSD, Novartis, Pfizer, Trevi, UCB and VielaBio. C.S, C.E.B and E.R are employees of and own stock in Eli Lilly and Company. AP is an Investigator for Anaptysbio, Eli Lilly, Incyte, Janssen, Krystal Bio, Lenus, Regeneron and UCB, a consultant for Abbvie, Abeona, Almirall, Amagma, Anaptysbio, Arena, Bausch, Bristol Myer Squibb, Dermavant, Dermira, Eli Lilly, Exicure, Forte, Leo, Lifemax, Phoenix, Pierre Fabre, Pfizer, Rapt, Regeneron, Sanofi, Sol-Gel, UCB and Venthera, and on the Data Safety Monitoring Board for AbbVie and Galderma.

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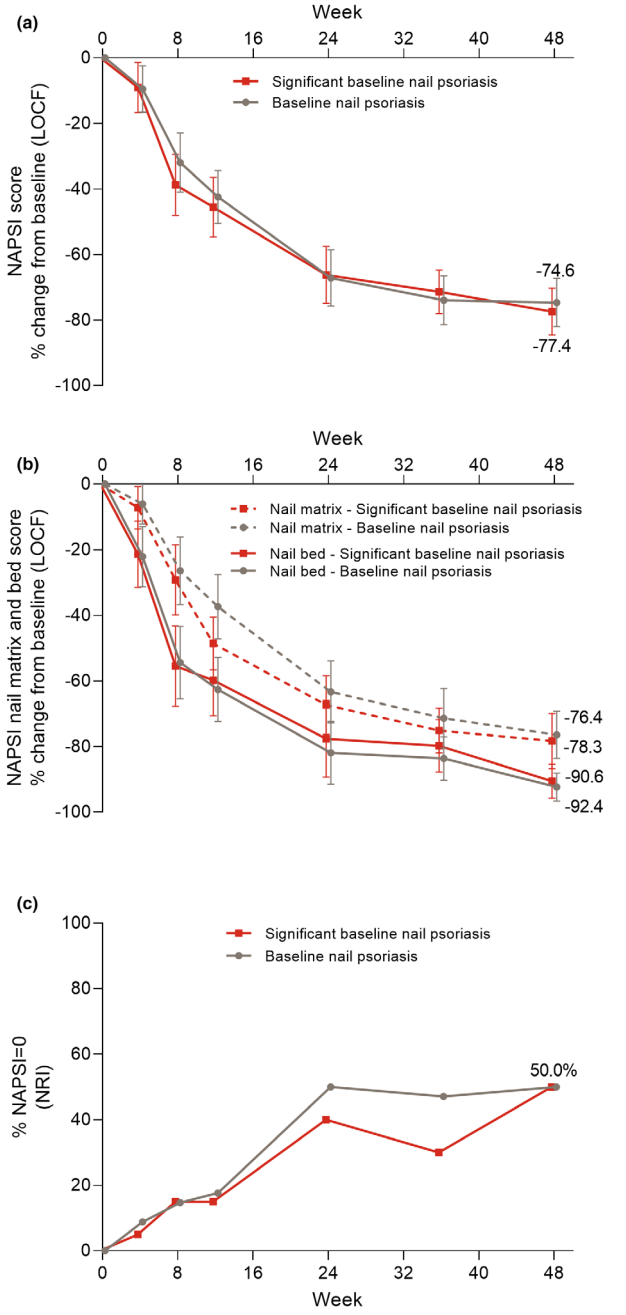

Figure 1 Improvement in overall Nail Psoriasis Severity Index (NAPSI) score, nail bed and nail matrix features and complete clearance of NP in paediatric patients treated with IXE over 48 weeks. Grey line denotes baseline NP (NAPSI ≥ 1; *N* = 34) and red line the subgroup with significant baseline NP (NAPSI ≥ 16 and ≥4 fingernails involved; *n* = 20/34). Mean (±standard error) percentage (%) change from baseline in NAPSI score (a) and individual nail bed and nail matrix scores (b) were calculated via analysis of covariance (ANCOVA), with missing data imputed using modified baseline observation carried forward (LOCF) for patients with baseline and significant baseline NP. The proportion of patients achieving complete clearance in their NP (NAPSI = 0) (C) are shown and calculated via non-responder imputation (NRI). Dotted lines represent nail matrix scores, and straight lines represent nail bed scores (b). Placebo to week 12 was not included due to the small number of patients with NP in patients given placebo. Descriptive statistics determined the percentage mean change from baseline in NAPSI score (global score; individual nail matrix and nail bed scores) and the proportion of patients reaching complete clearance (NAPSI = 0) through 48 weeks of IXE treatment.

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