

LETTER TO THE EDITOR

Treatment of chronic hand eczema with dupilumab—A retrospective follow-up study

To the Editor,

Only few therapeutic options are available for chronic hand eczema (CHE), and a significant proportion of CHE patients do not achieve sufficient disease control, emphasizing the need for new therapeutic options.^{1,2} Previous studies have shown that the IL-4/IL-13 inhibitor, dupilumab, is an effective treatment for atopic CHE, and case reports have indicated that CHE patients without atopic dermatitis (AD) may also benefit from dupilumab.^{3–6} Here, we present retrospective data from the first 19 adult CHE patients treated with dupilumab at two Danish dermatological departments.

Patients with a diagnosis of CHE and a dupilumab prescription in the electronic patient record system, Sundhedsplatformen/Epic, were identified from the dermatological departments at Bispebjerg Hospital and Gentofte Hospital, Denmark. Data on demographics, CHE subtype and previous treatments were extracted from the patient's medical records. As patient-reported outcomes, the following questions were included:

'After you initiated treatment with dupilumab did you experience: (1) improvement, (2) no change, (3) worsening of hand eczema?'

'After you initiated treatment with dupilumab did you experience: (1) improvement, (2) no change, (3) worsening of quality of life?'

'Have you experienced any side effects after you initiated treatment with dupilumab (1) yes, (2) no—If yes, which side-effects did you experience?'

Fisher's exact tests were used to test for differences in self-reported improvement in CHE severity and HR-QoL (improved, unchanged and worsened) between subtypes.

Nineteen CHE patients receiving a standard dose of dupilumab were included in the study. All patients had previously been treated with systemic immunosuppressants (Table 1). Hyperkeratotic CHE was the most common CHE subtype ($n = 10$), and 6 patients (31.6%) had current or previous AD (Table 2). Overall, 14 patients (73.7%) reported improvement of CHE severity and HR-QoL while 5 patients (26.3%) reported unchanged or worsened clinical severity/HR-QoL. When stratified by CHE subtypes, all patients reporting

TABLE 1 Self-reported side effects and prior systemic therapies

Side effects	
Yes, n (%)	8 (42.1)
Ocular ^a , n (%)	4 (26.7)
Gastrointestinal ^b , n (%)	4 (26.7)
Headache, n (%)	2 (13.3)
Joint pain/inflammation ^c , n (%)	2 (13.6)
Fatigue, n (%)	1 (6.7)
Nausea, n (%)	1 (6.7)
Facial dermatitis, n (%)	1 (6.7)
Prior systemic therapies	
Number of prior systemic therapies, median (range)	3 (1–9)
≥2 therapies, n (%)	15 (78.9)
≥5 therapies, n (%)	7 (36.8)
Methotrexate, n (%)	12 (18.2)
Acitretin, n (%)	6 (9.1)
Alitretinoin, n (%)	12 (18.2)
Ciclosporine, n (%)	5 (7.6)
Prednisolone, n (%)	6 (9.1)
Azathioprine, n (%)	11 (16.7)
Mycophenolate mofetil, n (%)	7 (10.6)
Adalimumab, n (%)	3 (4.5)
Ustekinumab, n (%)	1 (1.5)
Ixekizumab, n (%)	1 (1.5)
Guselkumab, n (%)	1 (1.5)
Secukinumab, n (%)	1 (1.5)

^aConjunctivitis $n = 2$, recurrent corneal erosions $n = 1$, dry eyes $n = 1$.

^bDiarrhoea $n = 3$, increased flatulence $n = 1$.

^cJoint pain $n = 1$, tenosynovitis $n = 1$.

unchanged or worsened disease severity/HR-QoL had hyperkeratotic CHE (Table 2), and patients with hyperkeratotic CHE were significantly less likely to report improvement compared to all other subtypes (pooled) ($p = 0.033$). When stratified by AD status, 83.4% (5/6) of patients with current or previous AD reported improved severity/HR-QoL compared to 69.2% (9/13) of patients without a history of AD (Table 2).

Five patients (26.3%) with hyperkeratotic CHE discontinued dupilumab therapy due to insufficient response (Table 2),

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TABLE 2 Demographics and patient-reported outcomes stratified by hand eczema (HE) subtypes

	Subtypes						All subtypes
	Hyperkeratotic hand eczema	Atopic hand eczema	ACD	ICD	Pulpitis	Acute recurrent vesicular hand eczema	
Number of patients	10	4	2	1	1	1	19
Sex							
Female, <i>n</i> (%)	9 (90.0)	4 (100)	1 (50.0)	1 (100)	1 (100)	0 (0)	16 (84.2)
Male, <i>n</i> (%)	1 (10.0)	0 (0)	1 (50.0)	0 (0)	0 (0)	1 (100)	3 (15.8)
Age							
Years, mean	55.8	56.3	60.5	31.0	56.0	71.0	55.9 (13.0)
Self-reported change of hand eczema severity							
Improvement, <i>n</i> (%)	5 (50.0)	4 (100)	2 (100.0)	1 (100)	1 (100)	1 (100)	14 (73.7)
Unchanged, <i>n</i> (%)	3 (30.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (15.8)
Deterioration, <i>n</i> (%)	2 (20.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (10.5)
Self-reported change of health-related quality of life							
Improvement, <i>n</i> (%)	5 (50.0)	4 (100)	2 (100.0)	1 (100)	1 (100)	1 (100)	14 (73.7)
Unchanged, <i>n</i> (%)	3 (30.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (15.8)
Deterioration, <i>n</i> (%)	2 (20.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (10.5)
Current or history of atopic dermatitis							
Atopic dermatitis, <i>n</i> (%)	1 (10.0)	4 (100)	1 (50.0)	0 (0)	0 (0)	0 (0)	6 (31.6)
Number of prior systemic therapies							
Median [min-max]	5 [1-9]	2 [1-2]	4 [3-5]	2	1	4	3 [1-9]
Discontinuation of dupilumab							
<i>n</i> (%)	5 (50.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (26.3)
Time to dupilumab discontinuation							
Weeks, median [min-max]	8 [5-21]	NA	NA	NA	NA	NA	8 [5-21]
Self-reported side effects							
<i>n</i> (%)	5 (50.0)	2 (50)	0 (0)	0 (0)	0 (0)	1 (100)	8 (42.1)

Abbreviations: ACD, allergic contact dermatitis; CHE, hand eczema; ICD, irritant contact dermatitis.

and 8 patients (42.1%) reported mild side effects including ocular and gastrointestinal side effects (Tables 1 and 2).

Taken together, our data suggest dupilumab to be an effective treatment for patients with refractory CHE, including patients with no history of AD. However, the finding that patients with hyperkeratotic CHE were significantly less likely to report improvement implies that the clinical response to dupilumab may vary between CHE subtypes. It has been discussed whether hyperkeratotic CHE should be perceived as a distinct disease entity or a variant of psoriasis,⁷⁻⁹ potentially explaining the lower response rate to dupilumab in these patients. However, the finding that 50% of patients with hyperkeratotic CHE responded to dupilumab suggests Th2-driven inflammation in some patients with hyperkeratotic CHE highlighting the heterogeneity in molecular phenotype. Only one cohort study has evaluated the effectiveness of dupilumab in CHE patients without AD.¹⁰ The study included 15 patients with vesicular HE of which 40% and 60% experienced complete and partial response, respectively. Despite being limited by a high percentage

(46.6%) of patients having concomitant palmo-plantar psoriasis, the results are in line with findings in our cohort, emphasizing that dupilumab is also effective in CHE patients without AD.

In conclusion, dupilumab seems to be a promising therapeutic option for refractory CHE, both in patients with and without AD. Clinical trials are needed to support this conclusion.

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CONFLICT OF INTEREST

C.M.O.: Industrial postdoc at Leo Pharma. C.Z. has been a scientific consultant, advisor, investigator and speaker for Eli Lilly, Jansen Cilag, Novartis, AbbVie, Takeda, Amgen, Almirall, CSL, UCB, Regeneron, MSD, Leo Pharma. T.A. has been a speaker/investigator/advisor for AbbVie, Eli Lilly, LEO Pharma, Pfizer, Regeneron and Sanofi-Genzyme. Dr. Thyssen is an advisor for AbbVie, Almirall, Arena Pharmaceuticals, Coloplast, OM Pharma, Aslan

Pharmaceuticals, Union Therapeutics, Eli Lilly & Co, LEO Pharma, Pfizer, Regeneron and Sanofi-Genzyme, a speaker for AbbVie, Ammirall, Eli Lilly & Co, LEO Pharma, Pfizer, Regeneron and Sanofi-Genzyme, and received research grants from Pfizer, Regeneron, and Sanofi-Genzyme. Y.T.O., T.T.L. and T.S.P.: none to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

All patients received oral information of the study and provided informed consent.

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