[4]Dermatology Department, an UCARE Center, Faculdade de Medicina do ABC, Santo André São Paulo, Brazil
*E-mail: Pincelli.Thais@mayo.edu

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Real-world experience of dupilumab in the treatment of moderate-to-severe atopic dermatitis

Dear Editor,

Atopic dermatitis (AD) is a chronic inflammatory skin condition marked by intense, persistent pruritus and epidermal barrier dysfunction.[1,2] Dupilumab is a monoclonal antibody that inhibits IL (interleukin)-4 and IL-13, resulting in the downregulation of epidermal proliferation and inflammatory mediators, consequently promoting normalization of the skin.[3] Clinical trials have demonstrated the efficacy of dupilumab treatment in AD and supported an acceptable side effect profile.[1,4] There is currently limited evidence for its use in real-world clinical practice.[5–9] Therefore, the aim of this study is to analyze the safety and efficacy of dupilumab in a real-world Canadian dermatology practice.

A retrospective chart review was conducted at a dermatology clinic in Ontario, Canada, from September 2018 to June 2019. Patients were included if they had moderate-to-severe AD and received at least one dose of dupilumab. At the prescriber's discretion, some patients received concomitant topical or systemic treatment in addition to dupilumab for the optimal control of symptoms. All patients were administered a 600 mg loading dose of dupilumab given by subcutaneous injection, followed by 300 mg every 2 weeks. Safety was assessed by recording adverse events (AEs). An evaluation of overall response to treatment was done with a description of patient satisfaction and clinical response recorded in the patient's clinical chart at each visit.

Baseline characteristics of 34 patients in this study cohort are outlined in Table 1. Of the 34 patients analyzed, 20 (58.9%) reported an AE (Table 2). There was an average of 1.5 ± 1.6 AEs reported per patient on dupilumab. The most frequently reported AEs included nasopharyngitis (n = 4, 11.8%) and conjunctivitis (n = 4, 11.8%). Dupilumab was discontinued in two patients: one due to persistence of the disease and the other due to an AE of the development of swollen glands, otalgia, and myalgias.

Of our cohort, 33/34 showed some clinical improvement upon initiating dupilumab. Although most patients demonstrated

Table 1 Characteristics of the study cohort of patients treated with dupilumab (n = 34)

Variable	Value (%)
Sex, *N* (%)	
Female	20 (58.8)
Age, mean ± SD, years	
Mean age	50.1 ± 13.4
Dose administered	
Biweekly 300 mg subcutaneous injections	34 (100)
Duration on dupilumab administration	
Mean duration ± SD, years	1.8 ± 1.4
Shortest duration, years	0.1
Longest duration, years[a]	4.5
No of previously failed therapies, mean ± SD	4.8 ± 2.0
Topical therapies failed prior to dupilumab first dose, *N* (%)	
Topical corticosteroids	34 (100)
Tacrolimus	18 (53)
Calcipotriol	4 (12)
Pimecrolimus	3 (9)
Crisaborole	3 (9)
Conventional systemic therapies prior to dupilumab first dose, *N* (%)	
Methotrexate	19 (56)
Prednisone	17 (50)
Phototherapy	17 (50)
Cyclosporine	15 (44)
Antihistamine	9 (26)
Triamcinolone acetonide (intramuscular)	7 (21)
Alitretinoin	6 (18)
Azathioprine	3 (9)
Apremilast	2 (6)
No of concomitant therapies with dupilumab, mean ± SD	1.7 ± 0.9
Concomitant topical therapies with dupilumab *N* (%)	
Topical corticosteroids	26 (76)
Tacrolimus	10 (29)
Calcipotriol	1 (3)
Crisaborole	3 (9)
Concomitant systemic therapies with dupilumab *N* (%)	
Methotrexate	6 (18)
Antihistamine	6 (18)
Prednisone	1 (3)
Cyclosporine	1 (3)
Phototherapy	1 (3)
Alitretinoin	1 (3)

SD, standard deviation.
[a]Includes patients who completed a dupilumab clinical trial.

Table 2 Safety outcomes of patients treated with dupilumab ($n = 34$)

Variable	Value (%)
Reported AEs per patient, *N* (%)	
0	14 (41.2)
1	5 (14.7)
2	4 (11.8)
3	7 (20.6)
4	3 (8.8)
5	1 (2.9)
Mean ± SD	1.5 ± 1.6
AEs reported >1, *N* (%)	
Nasopharyngitis	4 (11.8)
Conjunctivitis	4 (11.8)
Hypertension exacerbation	3 (8.8)
Chest pain	2 (5.9)
Injection site reaction	2 (5.9)

AE, adverse events; SD, standard deviation.

a positive response, formal objective assessments were not completed for all patients. Clinical response to dupilumab was generally performed with the use of a global assessment scale to describe the overall appearance of the skin lesions (described as clear, almost clear, mild, moderate, or severe). There were variations in the degree to which the AD was controlled which may have been related to patient variability in the use of concomitant therapies.

Our results confirm that dupilumab provides promising clinical improvement in patients suffering from moderate-to-severe AD in real-world practice. In regards to safety, in this cohort, 11.8% of patients reported nasopharyngitis and 11.8% reported conjunctivitis compared to 15.7% and 8.0%, respectively, in clinical trials.[10] Moreover, 5.9% of patients reported injection site reactions compared to 13.2% of patients in clinical trials.

Our main study limitation is that of small numbers, and because our study was conducted in a busy community practice, it was not practical to measure objective indices of efficacy such as eczema area and severity index (EASI) and Scoring AD (SCORAD) for each patient at every visit. There are also inherent limitations of chart reviews which can be a threat to both internal bias (confounding bias) and external validity.

In conclusion, in real-world practice, our evaluation of dupilumab indicates that its use has both a lack of serious adverse effects and provides clinical improvement in a majority of patients with moderate-to-severe AD. Furthermore, in the context of the coronavirus disease 2019 (COVID-19) pandemic, the European Task Force on Atopic Dermatitis (ETFAD) has expressed that the use of dupilumab should be preferred over conventional systemic immune-suppressive treatments for the management of AD.[11] We support the clinical value of dupilumab as a promising therapy for the treatment of AD in our current landscape.

Nicole S. Kim [1], MD
Khalad Maliyar [1], BA
Luciana Oliveira [2], MD
Ashley O'Toole [1], MD
Melinda J. Gooderham [1]*, MD

[1]SKiN Centre for Dermatology, Probity Medical Research, Peterborough, ON, Canada, and [2]Department of Dermatology, Fortaleza Geeneral Hospital, Center University, Fortaleza, Ceara, Brazil
*E-mail: mgooderham@centrefordermatology.com

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The predictive value of β2-microglobulin for steroid resistance in children with Henoch-Schönlein purpura nephritis

Dear Editor,

Henoch-Schönlein purpura (HSP) is the most common systemic vasculitis in childhood and is characterized by palpable purpura, abdominal pain, arthritis, and renal disease. About 50% of children with HSP develop nephritis, mainly manifested by microscopic hematuria with or without mild proteinuria. Most cases achieve complete remission of nephritis, but in a small number of children, they progress to end-stage renal disease (ESRD).[1] Early steroid treatment is most appropriate for children with renal involvement.[2] However, steroids are not always effective, as a small proportion of children with Henoch-Schönlein purpura nephritis (HSPN) do not respond to steroids.[3]

β2-Microglobulin (β2-MG) is freely filtered at the glomerulus and reabsorbed in the proximal tubule. Therefore, elevated β2-MG in urine may indicate impaired tubular reabsorption.[4] This study aims to preliminarily assess tubular proteinuria as a predictor to identify steroid resistance.

This is a retrospective study. The medical records of inpatients younger than 16 years of age admitted to the Department of Dermatology of our hospital and firstly diagnosed with HSP from 2015 to 2020 were reviewed to identify children with HSPN. The diagnosis for HSP follows the European League Against Rheumatism/Paediatric Rheumatology International Trials Organization/Paediatric Rheumatology European Society criteria.[5] HSPN is determined by HSP plus proteinuria and/or hematuria. In our hospital, urinary β2-MG levels are routine laboratory tests (immunoturbidimetry, the positive evaluation criteria were β2-MG $\geq$0.3 mg/l) performed on inpatients with renal involvement before treatment. Patients who had been treated with steroids or immunosuppressants prior to admission and patients without records of urinary β2-MG were excluded from the analysis. A total of 243 patients (137 males and 106 females; age, 3–14 years; mean age, 6.8 years) with HSPN were included in this study. All had non-thrombocytopenic purpura, hematuria, and proteinuria. In the severity assessment conducted by the outpatient doctor, it was considered necessary for them to receive intravenous medication in the hospital due to moderate to severe proteinuria and/or hematuria, or persistent mild abnormalities in repeat urinalyses. Upon admission, all patients were treated with supportive care and intravenous methylprednisolone (initially 1–2 mg/kg/d, then slowly reduced to the minimum dose with the total course of 1–2 weeks). When discharged, 220 cases had complete resolution of symptoms and negative dipstick proteinuria for two times after 1–2 weeks of intravenous methylprednisolone without any immunosuppressant. For the purposes of this study, these patients were divided into steroid-resistant and steroid-responsive groups. Twenty-three patients who continued to have positive dipstick proteinuria (with or without rash) despite treatment with methylprednisolone, or had disease recurrence (mainly refers to recurrence of renal disease including proteinuria and/or hematuria, which may be accompanied by recurrence of skin, gastrointestinal, and/or joint involvement) on steroid tapering were transferred to pediatrics, nephrology, or other hospitals for further treatment after 2 weeks. These 23 patients were included into the steroid-resistant group. All continuous data were presented as the mean $\pm$ standard deviation, and differences between groups were analyzed by Student *t*-test. Chi-squared tests were used to compare categorical data. $P < 0.05$ was considered statistically significant. Table 1 shows that there was no statistically significant difference of age ($P = 0.680$) and sex ($P = 0.648$) between the two groups. As is shown in Table 2, there was statistical difference between two groups ($t = 5.45$, $P < 0.001$). The urine levels of β2-MG were significantly higher in the study group than in the control group.

HSPN has the potential for serious morbidity, and continuous proteinuria itself is at risk for progression to ESRD. Accurate prediction of response to steroid treatment is necessary to optimize HSPN treatment. In this study, the level of urinary β2-MG was higher in steroid-resistant patients, and there was statistically significant difference compared with steroid-responsive patients. Thus, we propose that urine β2-MG may be a predictor of HSPN in children's response to steroid treatment. The good correlation between β2-MG and steroid-resistant HSPN may help determine which patients require early referral to