studies demonstrating the success of increased κ-opioid receptor expression and butorphanol use for intractable pruritus associated with inflammatory skin conditions and systemic diseases.[1,4] The most common adverse effects associated with butorphanol use include sedation, psychomotor impairment, and nausea and vomiting (Supplemental Table I, available via Mendeley at https://data.mendeley.com/datasets/pgt6tcyjp6/1). Butorphanol is a controlled substance with the potential for dependency and is thus not recommended in patients with substance use disorders.[5]

Limitations of this study include the small sample size, inconsistency in patient compliance, and the open label study design. Future large-scale trials are needed to assess the safety and efficacy of intranasal butorphanol and to determine which types of chronic pruritus benefit most from treatment.

Raveena Khanna, BA,[a,b] Christina D. Kwon, MD,[a] Sagar P. Patel, MD,[a] Micah Belzberg, MD,[a] Kyle A. Williams, BS,[a] Ramona Khanna,[a] Emily Boozalis, MD,[c] and Shawn G. Kwatra, MD[a]

From the Department of Dermatology, Johns Hopkins University School of Medicine, Baltimore, Maryland[a]; the Creighton University School of Medicine, Omaha, Nebraska[b]; and the Division of Dermatology, David Geffen School of Medicine at the University of California, Los Angeles, Los Angeles, California.[c]

Authors Khanna and Kwon contributed equally to this manuscript as cofirst authors.

Funding sources: Dr Kwatra has received the Dermatology Foundation Medical Dermatology Career Development Award.

Conflicts of interest: Dr Kwatra is on the scientific advisory board for Incyte Corporation, Pfizer Inc, Regeneron Pharmaceuticals, and Menlo Therapeutics and has received grant funding from Galderma SA, Kiniksa Pharmaceuticals, and Pfizer Inc. Authors Khanna, Khanna, and Williams and Drs Kwon, Patel, Belzberg and Boozalis have no conflicts of interest to declare.

IRB approval status: Approval was granted by the Johns Hopkins Medicine Institutional Review Board. Patient consent was not required.

Reprints not available from the author(s).

Correspondence to: Shawn G. Kwatra, MD, Cancer Research Building II, Johns Hopkins University School of Medicine, Ste 206, 1550 Orleans St, Baltimore, MD 21231

E-mail: skwatra1@jhmi.edu

REFERENCES

1. Dawn AG, Yosipovitch G. Butorphanol for treatment of intractable pruritus. *J Am Acad Dermatol*. 2006;54(3):527-531.
2. Kwatra SG, Ständer S, Kang H. PD-1 blockade—induced pruritus treated with a mu-opioid receptor antagonist. *N Engl J Med*. 2018;379(16):1578-1579.
3. Kumar K, Singh SI. Neuraxial opioid-induced pruritus: an update. *J Anaesthesiol Clin Pharmacol*. 2013;29(3):303-307.
4. Phan N, Lotts T, Antal A, Bernhard J, Ständer S. Systemic kappa opioid receptor agonists in the treatment of chronic pruritus: a literature review. *Acta Derm Venereol*. 2012;92(5):555-560.
5. United States Food and Drug Administration. STADOL® STADOL NS® (Butorphanol Tartrate) Nasal Spray. Briston-Myers Squibb. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2002/19890s17lbl.pdf. Accessed June 11, 2019.

https://doi.org/10.1016/j.jaad.2020.07.017

The role of dupilumab in the management of idiopathic chronic eczematous eruption of aging

To the Editor: Idiopathic chronic eczematous eruption of aging (CEEA) is a poorly studied subtype of eczema that affects individuals aged older than 50 years.[1,2] Although histopathology displays spongiotic dermatitis, these individuals lack a history of atopic dermatitis at any point in their past and present with a highly pruritic, subacute/chronic eczematous eruption affecting the extremities and trunk, with characteristic sparing of the face.[1,2] CEEA can be particularly disabling for older patients given its persistence, associated significant pruritus, and refractory nature to topical and systemic immunosuppressive medications.[2] Historically, patients are worked-up for other causes of an eczematous eruption, and CEEA is considered a diagnosis of exclusion.[3]

To date, we are aware of 1 case report demonstrating successful treatment of this condition with dupilumab.[1] To further explore this relationship, we evaluated 15 consecutive patients (exclusion <65 years old) with CEEA treated with dupilumab at the atopic dermatitis dose. Exclusion criteria were based on previous guidelines,[1] including history of atopic dermatitis earlier in life or other atopic disorders, pruritus without visible inflammatory skin disease, and other causes of aging-related eczematous eruptions (eg, cutaneous T-cell lymphoma, bullous pemphigoid, allergic contact dermatitis, drug eruption, and infection/infestation).

Table I summarizes demographic data of this cohort. The patients in our cohort were a mean

Table I. Demographics and treatment characteristics

Variable	Total patients (N = 15)
Demographics	
Age, y	
Mean (SD)	75 (8)
Range	66-88
Sex, No. (%)	
Female	10 (67)
Male	5 (33)
Race, No. (%)	
White	13 (87)
African-American	2 (13)
Other	0
Treatment history, No. (%)	
Topical corticosteroids	15 (100)
Oral corticosteroids	11 (73)
Intramuscular corticosteroids	1 (7)
Topical calcineurin inhibitors	11 (73)
Other systemic immunosuppressive therapies	2 (13)
Phototherapy	1 (7)

No., Number.

Table II. Treatment response and adverse effects with dupilumab

Variable	Total patients (N = 15)
Time to symptom improvement, No. (%)	
<2 weeks	0
2-4 weeks	9 (60)
4-6 weeks	4 (27)
6-8 weeks	2 (13)
Degree of improvement	
Pretreatment IGA, No. (%)	
0	0
1	0
2	0
3	4 (27)
4	11 (73)
Mean (SD)	3.73 (0.46)
Post-treatment IGA, No. (%)	
0	8 (53)
1	3 (2)
2	4 (27)
3	0
4	0
Mean (SD)	0.73 (0.88)
Body surface area	
Pretreatment, mean (SD), %	20 (15)
Post-treatment, mean (SD), %	2.6 (4)
Dupilumab-related adverse events	
Ocular surface disease	2 (13)
Facial redness	0
Other	1 (7)
None	12 (80)

IGA, Investigator Global Assessment; *No.*, number.

age of 75 (SD, 8) years, consisting of 67% women and 33% men. Previous treatments that had failed were a topical corticosteroid, in all patients, a topical calcineurin inhibitor in 73% (11 of 15), and systemic immunosuppressive therapy, phototherapy, or both, in 73% (11 of 15). Improvement of the condition was seen in 60% of the patients 2 to 4 weeks after commencing therapy with dupilumab, and 40% saw improvement between 4 and 8 weeks (Table II). All patients responded to dupilumab with a pretreatment mean Investigator Global Assessment of 3.73 (SD, 0.46) and body surface area of 20% (SD, 15%) and post-treatment mean Investigator Global Assessment of 0.73 (SD, 0.88) and body surface area of 2.6% (SD, 4%).

One patient in the study stopped dupilumab 4 weeks after starting the medication due to adverse effects of nausea and fatigue. She demonstrated 100% clearance, with no recurrence after 2 months. Ocular surface disease was observed in 2 patients, 1 of whom discontinued the medicine after 5 months due to this adverse effect despite sustained 100% clearance. All the patients who continued taking the medicine had a sustained response from the start date of dupilumab: 47% (7 of 15) between 8 and 12 months, 27% (4 of 15) after 4 to 8 months, and 27% (4 of 15) after 0 to 4 months.

Our patients demonstrated positive responses to dupilumab, and the treatment was well-tolerated for CEEA. In CEEA, the aging immune system undergoes a switch leading to a T helper cell 2—predominant response driving the eruption and pruritus.[3] Traditional treatments are not ideal, given that CEEA can be refractory to topical corticosteroids and systemic immunosuppressive medications (ie, methotrexate, cyclosporine) have a high associated risk of adverse effects in the elderly due to their associated comorbidities. Furthermore, given the high rate of polypharmacy among the elderly[4] with a high risk of medication interactions, dupilumab represents a promising and potentially safer therapeutic option in this population.

Neda Shahriari, MD,[a] Bruce Strober, MD, PhD,[b,c] and Mona Shahriari, MD[b,c]

From the Department of Dermatology, University of Connecticut, Farmington, Connecticut[a]; the Department of Dermatology, Yale University, New Haven, Connecticut[b]; and Central Connecticut Dermatology, Cromwell, Connecticut.[c]

Funding sources: None.

Conflicts of interest: Dr Strober receives honoraria as a consultant for AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, Janssen, LEO Pharma, Eli Lilly, Meiji Seika Pharma, Novartis, Pfizer, GlaxoSmithKline, UCB Pharma, Sun Pharma, Ortho Dermatologics, Regeneron, and Sanofi-Genzyme; is a speaker for AbbVie, Lilly, Janssen, and Ortho Dermatologics; receives a consulting fee as scientific director for the Corrona Psoriasis Registry; is an investigator for Dermavant, AbbVie, the Corrona Psoriasis Registry, Dermira, Cara, and Novartis; and receives an honorarium as Editor-in-Chief of the Journal of Psoriasis and Psoriatic Arthritis. Dr M. Shahriari receives honoraria as a consultant for AbbVie, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, and Regeneron; is a speaker for AbbVie, Lilly, and Janssen; and is an investigator for AbbVie, the Corrona Psoriasis Registry, Dermira, Cara, Dermavant, and Novartis. Dr N. Shahriari has no conflicts of interest to declare.

IRB approval status: Not applicable.

Reprints not available from the author(s).

Correspondence to: Neda Shahriari, MD, 21 South Rd, Farmington, CT 06032

E-mail: shahriari@uchc.edu

REFERENCES

1. Brummer GC, Wang LT, Sontheimer RD. A possible role for dupilumab (Dupixent) in the management of idiopathic chronic eczematous eruption of aging. *Dermatol Online J*. 2018;24(2):13030/qt55z1f6xh.
2. Summers EM, Bingham CS, Dahle KW, Sweeney C, Ying J, Sontheimer RD. Chronic eczematous eruptions in the aging. *JAMA Dermatol*. 2013;149(7):814-818.
3. Hendricks AJ, Yosipovitch G, Shi VY. Dupilumab use in dermatologic conditions beyond atopic dermatitis—a systematic review. *J Dermatolog Treat*. 2019:1-10. https://doi.org/10.1080/09546634.2019.1689227.
4. Jetha S. Polypharmacy, the elderly, and deprescribing. *Consult Pharm*. 2015;30(9):527-532.

https://doi.org/10.1016/j.jaad.2020.07.023

Systemic rituximab for the treatment of the indolent forms of primary cutaneous B-cell lymphomas: Data from the Spanish Primary Cutaneous Lymphoma Registry

To the Editor: Primary cutaneous follicle center B-cell lymphomas (PCFCLs) and primary cutaneous marginal zone B-cell lymphomas (PCMZLs) have an indolent clinical course but a high rate of skin recurrences. Rituximab has been used in cases where local treatment is not indicated, but most publications are limited to isolated cases or short series of patients[1-4] (Supplemental Tables I and II, available via Mendeley at https://doi.org/10.17632/83r5x758gh.2).

This study evaluated the clinical response and tolerability of systemic rituximab as monotherapy in a prospectively monitored cohort of patients from the Spanish Primary Cutaneous Lymphoma Registry (RELCP).

The study included 54 patients (17 women), 29 with PCFCL and 25 with PCMZL. Patient characteristics are summarized in Table I. The median age at diagnosis was 54 years, and median follow-up was 90 months.

All patients received 4 intravenous weekly infusions of rituximab at a standard dose of 375 mg/m^2/d. The overall response rate, complete response (CR), partial response, stable disease, time to progression, progression-free survival (PFS), and time to next treatment (TTNT) were evaluated according to the Olsen criteria.[5] The overall response rate was 98%. There were 37 patients (68%) who achieved a CR (21 PCFCL and 16 PCMZL), 16 (30%) showed a partial response, and 1 (2%) had stable disease. Among 5 patients with nodal involvement, 4 achieved CR and 1 partial response. There were no differences in overall response rate or CR between PCFCL and PCMZL. This is in contrast with previous observations suggesting a lower response rate for PCMZL.[1,2]

Cutaneous relapse or progression occurred in 24 patients (44%), 12 with PCFCL and 12 with PCMZL, with a median time to progression of 11 months. Of these, 16 were retreated with systemic rituximab, with a median of 4 additional infusions. Median PFS after the initial rituximab treatment was 62 months (78 for PCFCL and 58 for PCMZL). These differences did not reach statistical significance ($P = .1719$) (Fig 1). Median TTNT was 62 months. No associations were found in Cox regression models in PFS or TTNT regarding type of lymphoma, sex, age, extent of lesions, or previous treatment with intralesional rituximab.

Treatment was well tolerated. The most frequent adverse events were grade 1 and 2 infusion reactions and transient inflammatory changes over the skin lesions. Some patients showed inflammatory reactions over apparently unaffected skin suggesting occult extension beyond the affected areas.

To the best of our knowledge, this study represents the largest series published. Because it originates from a national multicenter prospective registry, these results probably represent the current