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Dupilumab use in allergic contact dermatitis

To the Editor: Dupilumab is an interleukin 4 (IL-4) receptor α (IL-4Rα) inhibitor indicated in recalcitrant moderate-to-severe atopic dermatitis (AD).[1] Although contact dermatitis is considered a helper T-cell 1 (T_H1 cell)—mediated process, certain allergens sensitize by induction of T_H2 pathways.[2] Our retrospective case-study suggests that dupilumab might be effective in the inhibition of weaker allergens that elicit a T_H2-mediated IL-4—dependent allergic contact dermatitis (ACD).

A retrospective chart review was performed to identify all patients treated with dupilumab for recalcitrant dermatitis by 2 dermatologists at their respective clinical sites (Center for Dermatology, PA, Florham Park, New Jersey, and Loma Linda Veterans Hospital, Loma Linda, California). Clinical evaluations had been performed by the respective dermatologist as part of the clinical management, using a modified physician global assessment. All patients had been assessed for body surface area (BSA) involvement, severity index, and itch at baseline and 10-12 weeks after starting dupilumab. The patients continued to receive clinical care on an as needed basis thereafter. No side effects were associated with dupilumab. Table I (available at http://www.jaad.org) depicts demographic and clinical information, including areas involved, patch-test proven allergen sensitivities, previous failed systemic therapies, and treatment outcomes of all 15 patients.

The majority of these adult patients had a history of childhood AD and current hand dermatitis (73%). Recalcitrant facial dermatitis was prevalent during the dupilumab treatment in a significant number of the cases. The percent BSA affected by dermatitis ranged 10%-80% (mean 48%), and the percent improvement after dupilumab ranged 70%-100% (mean 85%). A weak-negative ($R = -0.1181$, $R^2 = 0.0139$) correlation with patient age and weak-positive correlation with BSA ($R = 0.06$, $R^2 = 0.0038$) were associated with improvement on dupilumab. In all, the 15 patients had sensitivities to 46 distinct allergens. The most frequent clinically relevant allergens were cocamidopropyl betaine (CAPB) (40%), nickel (33%), oleamidopropyl dimethylamine (27%), *Myroxylon pereirae* (20%), and fragrance mix 1 (20%).

Most of these adult patients had AD, a predominant T_H2-axis immune disorder. It has been reported that inflamed atopic skin is predisposed to the development of T_H2-mediated contact sensitization to weaker potency allergens, such as fragrances, emulsifiers, and surfactants (eg, CAPB).[2,3] Of note, a recent report by Puza and Atwater described a patient who elicited a 1+ patch reaction to the potent sensitizer methylisothiazolinone rather than an indeterminant (+/-) reaction to the weaker allergen dimethylaminopropylamine (a precursor of CAPB) while on dupilumab for severe AD.[4] The role of IL-4 in ACD has been demonstrated by IL-4—knockout mice, which still have the ability to elicit contact sensitivities to oxazolone but not 2,4,6-trinitrochlorobenzene, a contact allergen with T_H2-mediated sensitization.[5]

Prevalent nickel sensitization was expected given the hapten's ubiquity and atopic hand dermatitis association.[2] However, the attenuation of nickel dermatitis was unanticipated and notably suggests that nickel sensitization can involve the elicitation of the T_H2/IL-4 pathway. The remarkable clinical and quality-of-life improvements achieved by this group of prior frequent flyer patients mirrors the dramatic impact of biologics on psoriasis. This study highlights the untapped potential of IL-4 inhibitors in the treatment of adult patients with a history of AD and recalcitrant and systematized ACD to certain allergens.[2]

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Growth in the cost of biologics in Medicare beneficiaries, 2013 to 2016

To the Editor: Prescription drugs are more than twice as expensive per capita in the United States than anywhere else in the world, largely because of exclusive marketing rights granted by the US Food and Drug Administration.[1] Biologic medications for psoriasis and other disorders have no true bioequivalent substitutes. Biosimilars and competing biologics are competitors but are not interchangeable. This distinction precludes automatic substitution at the point of sale and the price decrease associated with entry of generics.[2] As such, costs of biologics are likely driven by other market factors. We sought to determine how prices of biologics have changed over time in the United States.

We examined the pricing of 7 biologic medications used for psoriasis (adalimumab, etanercept, infliximab, and ustekinumab) and other disorders (rituximab, abatacept, and omalizumab). Data from the Centers for Medicare and Medicaid Services' (CMS) Part D 2013-2016 Public Use Files[3] were analyzed, including prescriber specialty and state, prescription year, and geographic region (Table I). Mean drug cost per day of medication was determined to account for different dosing by indication. This was defined as the cost of dispensed drug divided by the aggregate number of day's supply dispensed. Prices were adjusted for inflation to 2016 US dollars using the Bureau of Labor Statistics' Consumer Price Index[4] and compared between years for each biologic medication (Fig 1).

Table I. Characteristics of biologic prescribers and prescriptions

Variable	Prescriber frequency	Claim frequency
Prescriber type, n (%)		
Rheumatology	35,267 (44.9)	1,789,485 (63.6)
Allergy/immunology	847 (1.1)	19,757 (0.7)
Dermatology	10,771 (13.7)	223,595 (7.9)
Family practice	2950 (3.8)	182,481 (6.5)
Gastroenterology	9081 (11.6)	306,809 (10.9)
Internal medicine	9339 (11.9)	95,909 (3.4)
Nurse practitioner	3504 (4.5)	3504 (4.5)
Physician assistant	3615 (4.6)	91,169 (3.2)
Other	3106 (4.0)	60,195 (2.1)
Region, n (%)		
South	29,087 (37.1)	1,110,180 (39.4)
Midwest	16,954 (21.6)	603,653 (21.4)
Northeast	16,397 (20.9)	533,393 (19.0)
West	16,040 (20.4)	567,322 (20.2)
Year, n (%)		
2013	16,615 (21.2)	639,084 (22.7)
2014	18,590 (23.7)	707,403 (25.1)
2015	20,948 (26.7)	717,172 (25.5)
2016	22,325 (28.5)	750,889 (26.7)

The most frequent biologic prescribers were rheumatologists. Dermatologists were the second most frequent biologic prescribers; however, there were more biologic prescriptions for gastrointestinal than dermatologic indications. The number of prescribers increased each year between 2013 and 2016, with providers from the South most likely to prescribe biologics. Adalimumab and etanercept were the least expensive of the psoriasis biologics across all years, with abatacept and omalizumab being the least expensive overall.

Significant price increases were observed for all biologics. Adalimumab had the highest annualized growth rate (18.1%) while rituximab had the lowest (2.3%). Ustekinumab was initially the most expensive biologic drug for psoriasis in 2013 but was overtaken by infliximab in 2015 to 2016.

Table I. Demographics of systematized patch test confirmed allergic contact dermatitis patients

Patient no.	Patient age when dupilumab initiated, y	Sex	History of childhood atopic dermatitis	Hand involvement	BSA at onset of dupilumab, %	Estimated % improvement within 10-12 wk on dupilumab	Recalcitrant dermatitis sites while on dupilumab	Previously failed systemic therapies
1	28	F	Yes	Yes	55	95	Hands, feet	CysA, pred
2	29	M	Yes	Yes	65	80	Face	MM, CysA, methotrexate, pred
3	35	M	Yes	Yes	50	80	Face, arms, hands	CysA, apremilast, AZA, pred
4	44	F	Yes	Yes	15	80	Face	MM, pred
5	53	M	No	No	65	100	Legs	CysA, pred
6	54	F	Yes	Yes	45	80	Face	CysA, MM, methotrexate, pred
7	54	M	Yes	No	30	90	Face, scalp	CysA, MM, pred
8	55	F	Yes	Yes	55	90	Face, eyelids, chest, hands	MM, pred
9	56	F	Yes	Yes	50	80	Neck, face	CysA, pred
10	58	F	No	Yes	50	95	Face, eyelids, legs	CysA, ustekinumab, pred
11	58	F	No	Yes	25	85	Scalp, face, chest, arms, legs	CysA, ustekinumab, pred
12	60	M	Yes	Yes	60	90	Face, trunk, legs, hands	CysA, MM, pred
13	64	M	Yes	Yes	80	70	Arms, legs	CysA, MM, AZA, etanercept, pred
14	69	F	Yes	No	65	85	Face, eyelids, breast	CysA, MM, pred
15	72	F	No	No	10	80	Trunk	CysA, pred

AZA, Azathioprine; *BSA*, body surface area; *CysA*, cyclosporin A; *MM*, mycophenolic acid; *pred*, rescue prednisone >3 times per year.