

Dupilumab in Dermatology: Potential for Uses Beyond Atopic Dermatitis

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ABSTRACT

Dupilumab inhibits the interleukin-4 receptor subunit α and is FDA approved for treatment of moderate-to-severe atopic dermatitis. It is a relatively new drug, and whether it is efficacious for other diseases in dermatology is an area of increasing interest. We searched the literature and ClinicalTrials.gov database for uses of dupilumab beyond atopic dermatitis in dermatology and for ongoing studies on new uses for dupilumab. Off-label reports identified described use of dupilumab for several different dermatologic conditions, including allergic contact dermatitis, hand dermatitis, chronic spontaneous urticaria, prurigo nodularis, and alopecia areata. Overall, there is limited but promising data for dupilumab use beyond atopic dermatitis in dermatology. The relatively safe adverse effect profile of dupilumab may make it an option for certain recalcitrant diseases in dermatology, but further studies will be needed to assess its efficacy and determine its best possible use.

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INTRODUCTION

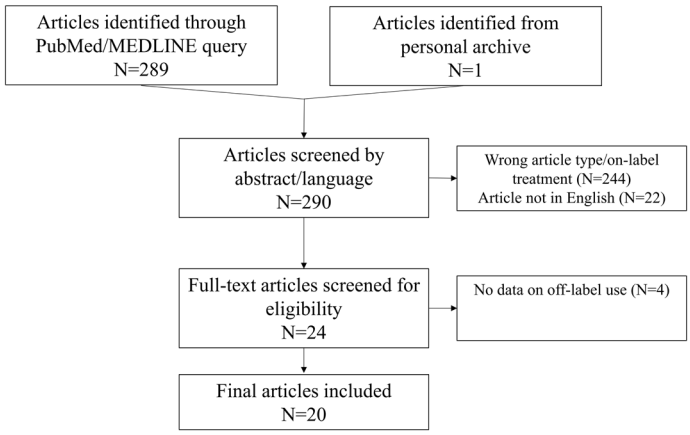
Dupilumab is an inhibitor of the interleukin (IL)-4 receptor subunit α (IL-4Rα), which prevents interaction of the T-helper 2 (Th2) cytokines IL-4 and IL-13 with their respective receptors. Its efficacy has been studied most in atopic dermatitis and asthma—diseases where Th2 type immune responses play central roles. It is the first biologic to receive FDA approval for atopic dermatitis. In general, dupilumab is well tolerated, with few serious adverse effects reported. Adverse effects can include nasopharyngitis, headache, conjunctivitis and injection-site reactions. In multiple clinical trials, patients on dupilumab had fewer skin infections compared to patients on placebo.[1–3] Other reported possible adverse events included a relationship between dupilumab administration and development of alcohol flushing in one case, transient skin erythema and peeling, and alopecia.[4–6]

Given that dupilumab is relatively well tolerated and has shown efficacy in diseases mediated by Th2 processes, a new topic of interest is whether dupilumab might prove effective in other conditions in dermatology.

MATERIALS AND METHODS

The PubMED/MEDLINE database was queried with the term "dupilumab." We screened individual abstracts to determine if there was use of dupilumab for a condition in dermatology besides atopic dermatitis. If unclear from the abstract, we screened the article text. Articles were required to be in English. We also queried the ClinicalTrials.gov database to search for ongoing studies of dupilumab in dermatology. Dupilumab dosing followed the standard regimen used for atopic dermatitis (600 mg loading dose, followed by 300 mg every 2 weeks) unless otherwise specified.

FIGURE 1. Article selection methodology for identifying articles containing dupilumab use in dermatology beyond atopic dermatitis.



RESULTS

Allergic Contact Dermatitis

In retrospective reviews of patients with allergic contact dermatitis treated with dupilumab, most achieved improvements in involved body surface area (BSA), decreases in investiga-

tor global assessment (IGA) scores, and in patient reported outcomes including pruritus (Table I). Many of these patients had histories of atopic dermatitis. In addition, the majority of patients that investigators treated with dupilumab for allergic contact dermatitis had moderate or severe baseline disease, with average baseline IGA scores of 3.2±0.7 (1 standard deviation) in one study and mean body surface area (BSA) involvement of 48 ± 19.9% in another study.[7,8]

Hand Dermatitis

Reports generally described improvements in hand dermatitis on dupilumab. Various types of hand dermatitis were described in articles including allergic contact dermatitis, atopic hand eczema, and dyshidrotic eczema. Cases where dupilumab was chosen for this indication involved severe baseline disease or recalcitrant cases (Table 1). The largest study included 38 patients with hand dermatitis of various etiologies. It reported that the majority of patients improved in terms of IGA scores, and in subjective reports of pruritus and pain from hand fissures (Table 1).[9] Isolated reports also describe successful use of dupilumab for highly recalcitrant hand dermatitis, resulting in improvement in patients who had previously failed multiple treatment modalities including oral immunosuppressants.[10]

Chronic Spontaneous Urticaria

One case series described 6 patients with histories of atopic dermatitis who failed omalizumab and were subsequently trialed on dupilumab, with all 6 patients sustaining improvement.[11] Dupilumab is now being studied in randomized clinical trials for chronic spontaneous urticaria (CSU) and cholinergic urticaria (Table 2).

Prurigo Nodularis

Small case series reported improvement in patients with prurigo nodularis in terms of subjective itch ratings, and in lesion number and size. In addition, concomitant therapies were able to be weaned (Table 1).

Alopecia

Four case reports describe response of alopecia to dupilumab, which all coincidentally improved in patients receiving dupilumab for atopic dermatitis. A randomized controlled trial is currently underway studying dupilumab for treatment of alopecia areata with and without atopic dermatitis.[12]

Miscellaneous

Isolated case reports describe successful use of dupilumab for eosinophilic annular erythema, anogenital pruritus, and bullous pemphigoid (Table I).

TABLE 1.

Dupilumab Use Beyond Atopic Dermatitis in Dermatology

Disease	Study Type (# of Patients)	Efficacy	Treatment Duration	Citation
Allergic contact dermatitis	Case series (2)	Marked improvement, from diffuse involvement to BSA involvement of 5% and 2% in each patient	4-6 months	Chipalkatti et al.[13]
Atopic dermatitis and concomitant allergic contact dermatitis	Retrospective re-view (17 diag-nosed by patch testing)	Average initial IGA of 3.2±0.7 (SD) to final IGA of 1.1±1.2 (SD), 57% with IGA of 0 or 1 after treatment, 82% with decrease in involved BSA, 23% with resolution of pruritus, 100% with improvement in pruritus	Variable	Chipalkatti et al.[7]
	Retrospective re-view (14 with a clinical diagnosis)	Average initial IGA of 3.3±0.5 (SD) to final IGA of 1.2±1.3 (SD), 73% with IGA of 0 or 1 after treatment, 83% with decrease in involved BSA, 33% with resolution of pruritus, 100% with improvement in pruritus		
Allergic contact dermatitis	Case series (3)	>90% improvement in involved BSA in all 3 patients	6-13 months	Goldminz & Scheinman[14]
Allergic contact dermatitis	Retrospective re-view (15 with positive patch testing, 11 with history of AD, 11 with hand derma-titis)	Mean baseline BSA 48±19.9% (SD); Estimated percent improvement from baseline: mean of 85% (range 70-100%)	>10-12 weeks	Machler et al.[8]
Allergic contact dermatitis	Case report (1)	Marked improvement within 8 weeks allowing discontinuation of myco-phenolate and tapering of prednisone dose	>4 months	Joshi & Khan[15]
Atopic hand eczema	Case report (1 patient with long history of AD)	Hand eczema severity score at 244/360 at baseline to 115 at week 4, 11/360 at week 16; prednisone suc-cessfully tapered from 7.5 mg/day to 0 at week 12 of treatment	>16 weeks	Oosterhaven et al.[16]

TABLE 1. (CONTINUED)

Dupilumab Use Beyond Atopic Dermatitis in Dermatology

Disease	Study Type (# of Patients)	Efficacy	Treatment Duration	Citation
Dyshidrotic eczema	Case series (2)	Marked improvement in palmar hy-perkeratotic plaques and fissures at week 8 in patient #1, complete reso-lution of erythema; complete resolu-tion at 4 months in patient #2 in palms and soles (dupilumab mainte-nance therapy started after cyclospor-ine bridge)	>2-4 months	Weston et al.[17]
Dyshidrotic eczema	Case report (1)	Complete clearance by 12 weeks	>12 weeks	Nanda et al.[18]
Hand eczema	Case series (3)	Complete clearance in 6 weeks in patient #1; 90% improvement at week 6 maintained to 8 months in patient #2; 80% improvement in hands main-tained to 8 months in patient #3	>3-8 months	Zirwas et al.[10]
Hand dermatitis (various etiologies)[a]	Retrospective re-view (38 total, 6 only with dermati-tis of the hands, 32 with dermatitis of hands and body)	Baseline IGA 3.26±0.72 (SD) to final IGA of 1.72±1.21 (SD), 40.0% achieved IGA of 0 or 1, 72% im-proved in terms of IGA decrease; in 30 patients reporting pruritus at base-line, 96.7% re-ported improvement, 26.7% reported resolution; in 6 pa-tients with dermatitis related pain and 11 with hand fissuring, 100% reported improvement	>3 months	Lee et al.[9]
Alopecia totalis	Case report (1 patient with AD covering 70% BSA)	Initial improvement in hair regrowth at week 6, at 11 months, terminal hair growth over nearly the entire scalp	>11 months	Penzi et al.[19]
Alopecia universalis	Case report (1 patient with AD)	Full hair regrowth at 8 months, par-tial regrowth of eye brows, no re-sponse in hair growth in any other regions	>8 months	Alniemi & McGevna[20]
Alopecia areata	Case report (1, patient with baseline EASI 14.9)	Baseline SALT score of 87.4, hair regrowth start-ing at 3 months, near full recovery at 6 months with SALT score 7 (change of -80.4)	>6 months	Darrigade et al.[22]
Bullous pemphigoid	Case report (1)	Resolution of all blisters at 3 months of therapy, maintained without relapse	>10 months	Kaye et al.[23]
Eosinophilic annular erythema	Case report (1)	Complete clearance of lesions by week 4 and resolution of pruritus	>5 months	Gordon et al.[24]
Chronic spontaneous urticaria with atopic dermatitis	Case series (6, all had failed omalizumab and all with history of AD)	Marked improvement in urticaria in all 6 patients, in 5/6 either resolution of urticaria or UAS score <3 achieved at 3 months on dupilumab (baseline UAS scores were 31-42 in cohort)	>3 months	Lee & Simpson[11]
Prurigo nodularis	Case series (3)	Improvement in lesion characteristics in all 3 patients over 12 weeks; re-duction in pruritus numerical scale rating from baseline 7-10 to 0-2 by week 12, all 3 patients able to wean other concomitant therapies	>12 weeks	Beck et al.[25]
Prurigo nodularis	Case series (4)	2 patients with baseline NRSi score of 10 de-creased to 0 at 3-month fol-low-up, 1 patient with baseline NRSi 6 decreased to 0 at 1 month, and 1 patient with baseline NRSi of 9 de-creased to 0 at 2 weeks	Variable	Mollanazar et al.[26]
Anal/genital pruritus	Case report (1)	95% decrease in patient reported itch by week 4 with complete resolution of perianal dermatitis	>12 months	Yang & Murase[27]

Abbreviations: AD = atopic dermatitis; BSA=body surface area; EASI = Eczema Severity Assessment Index; IGA = Investigator's Global Assessment; NRSi = numeric rating scale for itch intensity; SD = standard deviation; SALT = Severity of Alopecia Tool; UAS= urticaria activity score
[a]Etiologies including dyshidrotic eczema, atopic dermatitis, and contact dermatitis

TABLE 2.

New and On-Going Studies On Off-Label Dupilumab Use				
Disease	**Study Type**	**Number of patients (estimated or actual)**	**Study Number**	**Citation**
Alopecia Areata, with or without history of atopic dermatitis	RCT	54	NCT03359356	12
Chronic spontaneous urticaria	RCT	72	NCT03749135	28
Cholinergic urticaria	RCT	72	NCT03749148	29

Abbreviations: RCT = randomized controlled trial

DISCUSSION

The evidence for dupilumab use beyond atopic dermatitis in dermatology is limited, without any current published randomized controlled trials supporting efficacy for additional indications. Retrospective reviews suggest it may be helpful for allergic contact dermatitis and hand dermatitis. Several other reports identify potential uses including alopecia areata and CSU. With small case series and case reports, it is possible that there is positive selection bias for description of successful off-label use of dupilumab in dermatology, and real-world data on off-label dupilumab use overall is lacking.

However, this is a promising new drug that may eventually be shown to have efficacy for various conditions in dermatology. Reasonable potential applications include diseases where Th2 responses are important to disease pathophysiology and where an appreciable proportion of patients fail to respond to current therapies, such as chronic urticaria.[30] The case series of 6 patients with CSU who failed omalizumab but responded to dupilumab is highly interesting. If dupilumab is shown to be effective for CSU in the RCT currently in progress, many interesting questions follow. For example, CSU patients with low baseline serum total IgE levels tend to poorly respond to omalizumab, but whether response of chronic urticaria to dupilumab varies depending on baseline IgE levels remains to be answered.[31]

Dupilumab has a relatively safe side effect profile, and the increased rates of conjunctivitis seen with dupilumab use thus far have only been observed in patients with atopic dermatitis.[32,33] Its potential for further applications in dermatology in recalcitrant cases is a highly interesting topic, although cost is a significant limiting factor. Ultimately, many further clinical studies, and increased understanding of skin disease pathophysiology will help determine the best possible uses for dupilumab in dermatology.

DISCLOSURES

The authors report no conflict of interest.

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