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The Prevalence of Dupilumab-Associated Adverse Events Among Black and African American Adult Patients With Atopic Dermatitis: A Retrospective Chart Review

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INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease that characteristically demonstrates upregulation of type 2 immune responses, impaired skin barrier function, and increased *Staphylococcus aureus* colonization.[1,2] Intense and persistent pruritus is a defining feature of moderate-to-severe atopic dermatitis.[3] AD has canonically been thought of as a disease that starts in childhood and rarely persists into adulthood.[4] More recent work has shown that adult-onset AD is not an uncommon occurrence and that there is increasing evidence of lifelong, persistent disease that can extend beyond childhood.[5,6] There appear to be important racial differences in AD prevalence, incidence, severity, and persistence in the United States (US).[7] Indeed, African American (AA) and Latinx people in the US appear to experience higher rates of AD prevalence and disease burden.[8] The pathophysiology of AD also appears to have differences racially; FLG mutations are 6 times less common in AA patients compared to European American patients with AD.[7] Furthermore, while all ethnic groups of patients with AD have an immune phenotype characterized by strong T_H2 activation, there appears to be significant difference in immune phenotype polarization, wherein Asian patients with AD have stronger T_H17/T_H22 activation and AA patients with AD have the highest serum IgE levels and largely lack T_H1 and T_H17 activation.[7]

Dupilumab is an IgG-4 based monoclonal antibody specific for IL-4Rα that is approved by the US Food and Drug Administration (FDA) for the treatment of refractory, moderate-to-severe AD in patients aged 6 months of age and older.[9] Long-term real-world side effects of dupilumab, dupilumab-associated adverse events (d-AE), most commonly include ocular and cutaneous reactions.[10] Given the recent findings of ethnic differences in immunophenotype characterization, it is of clinical interest whether d-AE differ by ethnicity. We aim to identify the most frequently reported d-AE and investigate the relative risk between the prevalence of d-AE and race in a single-center, retrospective chart review.

The inclusion criteria for this retrospective chart review were males and females aged 18 or older with a past or current prescription for dupilumab to treat dermatologic conditions, seen in the clinic between January 1, 2017, and January 1, 2022. Specifically, we analyzed the charts of AD patients 18 and older, who were seen at a University of Pennsylvania Health System (UPHS). Our goal was to identify the most common side effects in our cohort of Black/AA patients treated with dupilumab. Patients were excluded if they did not meet the inclusion criteria or if they were on dupilumab for an investigational trial or an off-label indication. This study was approved by the University of Pennsylvania Institutional Review Board. Patient demographics can be seen in Table 1.

TABLE 1.

Patient Demographics	
Demographics (n=445)	
Race	Percent of sample size
Black/African American	29.21% (n=130)
Other SOC (Asian, Hispanic/Latinx, American Indian, etc.)	17.30% (n=77)
White	49.21% (n=219)
Unknown/Declined	4.27% (n=19)

Compared with clinical trials, our study population had a greater representation of Black/AA patients with dupilumab-treated AD, but a similar safety profile-with ocular manifestations as the most frequently reported d-AE (Table 2).[11,12] Most patients with AD did not report d-AE (79%, n=352). Of the 219 White patients, nearly 1 in 2 reported d-AE, whereas out of 130 Black/AA patients, only 1 in 3 reported d-AE. Our data found that Black/AA patients experienced a lower risk of having a d-AE (RR 0.78; 95% CI 0.46, 1.34; Table 3), however, it was not a statistically significant difference. The lack of statistical significance may be due to our small sample size.

TABLE 2.

Dupilumab-Associated Adverse Events (d-AE) by Adverse Events Category and Race								
Race	Ocular (%)	Derm (%)	MSK (%)	Inject. (%)	Allerg. (%)	Malig. (%)	Other	Total (%)
Black/African American	15 (60%)	3 (12%)	2 (8%)	4 (16%)	0 (0%)	1 (4%)	0 (0%)	25 (100%)
White	34 (67%)	6 (12%)	4 (8%)	5 (10%)	0 (0%)	0 (0%)	1 (8%)	51 (100%)
Other SOC	9 (75%)	2 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	12 (100%)
Unkn./Declin.	4 (80%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	5 (100%)

AE categories: ocular (conjunctivitis, blepharitis, dryness, irritation, etc.); dermatologic; MSK; Injection site; Allergic (anaphylaxis); other

TABLE 3.

Relative Risk (RR) of Dupilumab-Associated Adverse Events (d-AE) and OCULAR (d-AE) by Patient Race/Ethnicity				
Race	d-AE vs no AE		Ocular d-AE vs any/no d-AE	
	Full sample of patients (n=445)			
	RR	95% CI	RR	95% CI
White	ref		ref	
Black/African American	0.78	0.46, 1.34	0.71	0.37, 1.36
Other SOC	0.61	0.30, 1.21	0.72	0.33, 1.58
Unknown/Declined	1.18	0.40, 3.42	1.45	0.45, 4.64

Statistical Significance ($P<0.05$)

Atopic keratoconjunctivitis appears to be predominantly a Th-1 mediated response.[12] By blocking TH2 cytokines (IL-4/IL-13), dupilumab may result in an immune shift towards a Th-1 response, thereby increasing the risk of ocular d-AE. The lower level of ocular d-AE in Black/AA AD patients may be due to the relative paucity of Th-1 activation noted in AA AD patients.[7,13] Limitations of this study include our small sample size, narrow eligibility requirements, and that this study was limited to a single health system.

Our study suggests that patients of Black or African American background with dupilumab-treated AD may experience fewer adverse events than their White counterparts. Considering that diverse racial/ethnic representation is low in many dermatologic clinical trials, it is important to assess real-life outcomes of medication efficacy and safety outcomes in SOC patients. Larger datasets from multiple institutions are needed to assess whether these findings are statistically significant.

DISCLOSURES

Dr. Mollanazar has served as an advisory board member for Boehringer Ingelheim, Janssen, Novartis, Regeneron Pharmaceuticals Inc., Sanofi, Trevi Therapeutics, Menlo Therapeutics Inc., Galderma, Leo Pharma, AbbVie, Pfizer, and Beiersdorf; as an investigator for Sanofi, Regeneron Pharmaceuticals Inc., and Genzyme; and as a consultant for Novartis, Regeneron Pharmaceuticals Inc., Sanofi, Janssen, and AbbVie.

Dr. Taylor has served as a consultant, advisory board member, and/or speaker for AbbVie, Arcutis, Armis Scientific, Avita, Beiersdorf, Biorez, Bristol-Myers Squibb, Cara Therapeutics, Dior, Eli Lilly, EPI Health, Evolus, Galderma, GloGetter, Hugel America, Incyte, Johnson & Johnson, L'Oreal USA, MedScape, MJH LifeSciences, Pfizer, Piction Health, Sanofi, Scientis US, UCB, and Vichy Laboratoires. She has received royalties from McGraw-Hill. She has served as an investigator for Allergan, Concert Pharmaceuticals/Sun Pharma, Croma-Pharma GmbH, Eli Lilly, and Pfizer.

Dr. Temitayo Ogunleye has served as an advisory board member for Beiersdorf and as a speaker for MJH LifeSciences.

The other authors have no conflict of interest to disclose.

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