RESEARCH LETTER

Two-year efficacy, safety, and drug survival of dupilumab for atopic dermatitis: A real-world Canadian multicenter retrospective study

To the Editor: Limited studies are available on the long-term efficacy and safety of dupilumab for moderate-to-severe atopic dermatitis (AD) beyond the 52-week follow-up. A recent publication by our group showed favorable efficacy outcomes with no new safety signals in patients with AD over 52-weeks of dupilumab treatment.[1] An observational prospective cohort study of the TREAT NL (TREatment of ATopic eczema, the Netherlands) registry showed consistent safety and efficacy outcomes up to week 84.[2] Herein, we aimed to assess the 2-year drug survival of dupilumab in real-world patients with AD.

Following research ethics board approval, we conducted a multicenter retrospective cohort study of all consecutive adult patients (aged ≥18 years) receiving treatment with dupilumab at 3 tertiary academic dermatology clinics in Toronto. Cases

Table I. Reported adverse events and dupilumab discontinuation based on follow-up time

Variable	Follow-up periods		
	0-16 weeks (*N* = 145)	16-52 weeks (*N* = 143)	52-104 weeks (*N* = 139)
One or more adverse event, *n* (%)	64 (44)	48 (34)	31 (22)
Reported adverse events, *n* (%)			
Ocular surface disease	45 (31)	36 (25)	18 (13)
Infections	8 (6)	3 (2)	4 (3)
Oral herpes	6 (4)	1 (1)	2 (1)
Cellulitis	2 (1)	1 (1)	1 (1)
Cystitis	1 (1)	1 (1)	0
Flu-like symptoms	1 (1)	2 (1)	0
Upper respiratory tract infection	0	0	1 (1)
Skin disorders			
Injection site reaction	6 (4)	2 (1)	2 (1)
Head and neck eczema flare or redness	2 (1)	4 (3)	7 (5)
Urticaria	1 (1)	2 (1)	2 (1)
Asthma flare	1 (1)	0	0
Musculoskeletal			
Fatigue	1 (1)	0	0
Arthralgia	2 (1)	3 (2)	0
Headache	0	0	0
Gastrointestinal symptoms	4 (3)	2 (1)	0
Generalized nonspecific symptoms*	4 (3)	2 (1)	0
Dupilumab discontinuation, *n* (%)†	5 (3)	20 (14)	9 (6)
Secondary to adverse event	4 (3)	6 (4)	4 (3)
Due to lack of efficacy	1 (1)	12 (8)	1 (1)
Non–drug-related reason‡	0	2 (1)	4 (3)

n, Number of subjects meeting criteria.

*Nonspecific symptoms include episodes of dizziness, lightheadedness, blurred vision, and/or sweating.

†Patients who discontinued dupilumab due to an adverse event or lack of efficacy were carried forward and included as Investigator Global Assessment nonresponders for each timepoint. Discontinuation due to non–drug-related reasons was excluded from Investigator Global Assessment analysis.

‡Non–drug-related reasons include pregnancy, travel, and loss of insurance drug coverage.

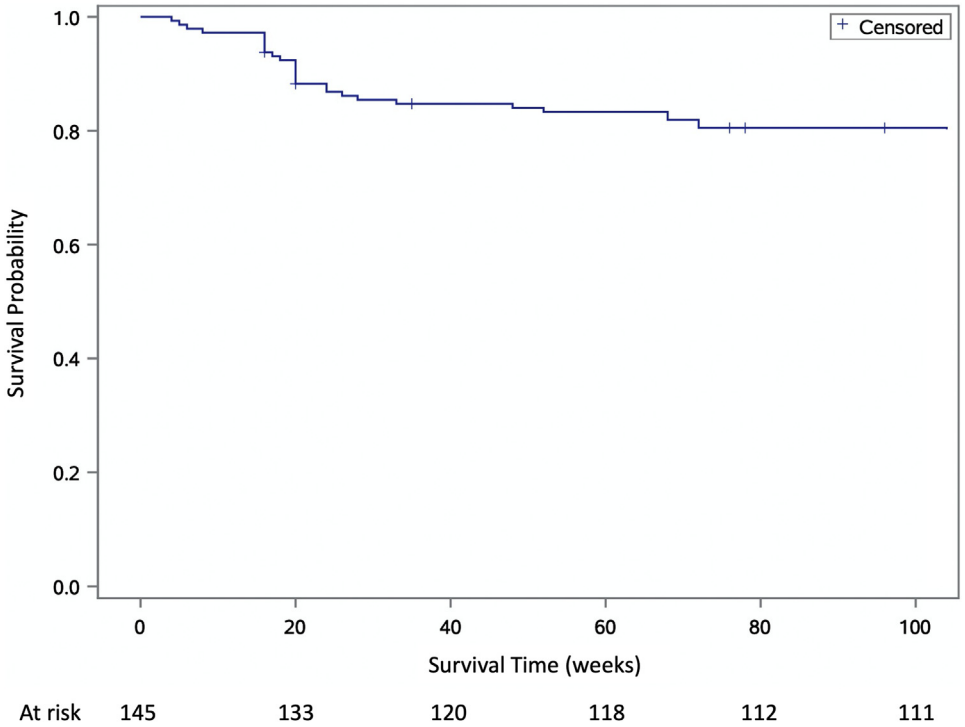

Fig 1. Unadjusted drug survival curves for patients with atopic dermatitis on dupilumab treatment. The graph shows the probability of discontinuation due to any cause, including lack of efficacy and adverse event. Of 139 patients, treatment was discontinued in 28 (20%), and among those in whom treatment failed, the median time to discontinuation was 20 weeks (95% CI, 28.7-11.3 weeks).

were included if they had moderate-to-severe AD (Investigator Global Assessment [IGA] 3 or 4) at baseline and seen 104 weeks after dupilumab initiation while on therapy. Drug survival was analyzed using unadjusted Kaplan-Meier survival analysis to estimate the risk of and time to discontinuation. Patients were censored if their reason to stop dupilumab treatment was unrelated to efficacy or safety (eg, loss of insurance coverage).

We included 145 patients. The mean (±SD) age was 44.5 ± 14.8 years, and 74 patients (51%) were female. Comorbid conditions included asthma (n = 97; 48.3%), allergic rhinitis (n = 38; 26.2%), and urticaria (n = 15; 10.3%). Patients had failed a median of 2 (range, 0-6) systemic therapies prior to dupilumab.

In total, 85 of 145 patients (59%), 83 of 143 (58%), and 94 of 139 (68%) achieved IGA 0 or 1 (clear or almost clear) at 16, 52, and 104 weeks, respectively. Of the 83 patients with IGA 0/1 at 52 weeks, 74 (89%) maintained IGA 0/1 at 104 weeks. Of the 60 patients with IGA >1 at 52 weeks, 20 (33%) achieved IGA 0/1 at 104 weeks.

In the entire cohort, 89 of 145 patients (61%) reported 1 or more adverse events (AEs) at any point throughout the study period (Table I). New or persistent AEs were reported by 64 of 145 patients (44%), 48 of 143 (34%), and 31 of 139 (22%) between 0 and 16, 16 and 52, and 52 and 104 weeks, respectively. Ocular surface disease was the most commonly reported AE between 52 and 104 weeks (18 of 139 patients; 13%). Drug survival of dupilumab was 97%, 83%, and 80% after 16, 52, and 104 weeks, respectively (Fig 1). Discontinuation of dupilumab treatment was most common between 16 and 52 weeks (20 of 143 patients; 14%) compared with that between 52 and 104 (9 of 139 patients; 6%) and 0 and 16 weeks (5 of 145 patients; 3%) (Table I).

The percentage of patients achieving IGA 0/1 at 104 weeks (68%) is comparable to rates seen in open-label extension studies of phase 3 randomized controlled trials at weeks 76 (57.8%) and 100 (58.1%).[3,4] The majority of patients with IGA 0/1 at 52 weeks maintained IGA 0/1 at 104 weeks (89%), and delayed response beyond 52 weeks was less common (33%). In further support of favorable long-term outcomes, all patients on a concomitant systemic therapy (cyclosporine, methotrexate, mycophenolic acid, or prednisone) for at least 12 weeks prior to initiating dupilumab treatment (n = 18; 12%) were able to stop that treatment before 104 weeks. Importantly, drug survival remained high (80%) at

104 weeks of treatment, with the majority of discontinuations occurring between 16 and 52 weeks due to lack of efficacy or AE. No new safety signals were identified beyond 52 weeks, with fewer patients reporting AEs compared with earlier in the treatment period. Limitations of this study include the lack of control arm and reliance on patient charts to assess outcomes.

Overall, these results support the long-term use of dupilumab to achieve sustained control of moderate-to-severe AD in real-world clinical practice.

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Conflicts of interest

Dr Drucker has received compensation from the British Journal of Dermatology (reviewer and section editor), American Academy of Dermatology (guidelines writer), and National Eczema Association (grant reviewer). He has been a paid consultant for the Canadian Agency for Drugs and Technology in Health. Dr Piguet has received honoraria or fees for consulting and/or speaking for AbbVie, Almirall, Celgene, Janssen, Novartis, and Pfizer and has received departmental support for Cardiff University from AbbVie, Almirall, Alliance, Beiersdorf UK Ltd, Biotest, Celgene, Dermal, Eli Lilly, Galderma, Genus Pharma, GlobeMicro, Janssen-Celag, LaRoche-Posay, L'Oreal, LEO Pharma, Meda, MSD, Novartis, Pfizer, Sinclair Pharma, Spirit, Stiefel, Samumed, Thornton Ross, TyPham, and UCB and for the University of Toronto from Sanofi. Dr Yeung has been a speaker, consultant, and investigator for AbbVie, Allergan, Amgen, Arcutis, Astellas, Bausch Health, Boehringer Ingelheim, Bristol Meyers Squibb, Celgene, Centocor, Coherus, Dermavant, Dermira, Forward, Galderma, GlaxoSmithKline, Incyte, Janssen, Kyowa, Leo Pharma, Lilly, Medimmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sandoz, Sanofi Genzyme, Sun Pharma, Takeda, UCB, and Xenon. Drs Georgakopoulos and Felfeli and author Jo have no conflicts of interest to declare.

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