

LETTER

Dupilumab has a profound effect on specific-IgE levels of several food allergens in atopic dermatitis patients

To the Editor,

Dupilumab is the first biological developed for atopic dermatitis (AD). It blocks the signaling pathway of Type 2 (T2)-related cytokines, IL-4 and IL-13, and might therefore also have an effect on other T2-related diseases, such as food allergy (FA).¹ AD has been shown to be a major risk factor for food sensitization and the development of immunoglobulin E (IgE)-mediated food allergy.^{2,3} Dupilumab treatment in AD patients reduces total serum IgE; however, the course of specific IgE (sIgE) levels for food allergens during dupilumab treatment has not been defined yet.¹ Therefore, the aim of this study was to investigate the effect of dupilumab on sIgE levels in patients with moderate-to-severe AD with comorbid food allergy.

Adult AD patients treated with dupilumab with a suggestive clinical history of food allergy (resp. peanut, hazelnut, almond, cashew nut, walnut, kiwi, and apple), and a corresponding positive sIgE (≥ 0.35 kU/L) at the start of treatment, were included. Data were extracted from the prospectively BioDay registry between October 2017 and February 2022. All patients provided written informed consent. Linear mixed models were used to model the development of sIgE values over time, providing median IgE values (with 95% CIs) and corresponding percentage decline. All analyses were performed for each food separately (detailed explanation of methods is described in the [Supporting Information](#)).

A total of 125 AD patients reporting 307 food allergies were included, with 2682 corresponding sIgE samples. Most patients were allergic to one ($n = 42$, 33.6%) or two foods ($n = 35$, 28.0%) ([Table 1](#)). Peanut and hazelnut (51.2% and 52.0%) were the most common causative foods.

An estimated sustained percentage decrease of sIgE levels was observed for all food allergens during dupilumab treatment, with a decrease ranging from 53.0% (95% CI: 46.3–59.7) for peanut extract

to 62.9% (95% CI: 57.0–68.8) for apple after 1 year, and from 80.5% (95% CI: 68.9–92.1) for walnut to 86.9% (95% CI: 78.7–95.2) for kiwi after 3 years of treatment ([Figure 1](#)). After 3 years, the lowest median sIgE levels were observed for almond (0.4, 95% CI: 0.2–0.6), while hazelnut had the highest median sIgE levels (3.0, 95% CI: 2.1–4.3) ([Figure S1](#)).

This is the first study that showed a profound decrease in sIgE levels of food allergens during dupilumab treatment (up to 3.5 years) in a large population of food-allergic AD patients. At present, there is no direct evidence that a decrease of sIgE levels leads to less clinical reactivity; however, several studies indirectly support that the decrease of sIgE levels could be a surrogate marker for the decrease of food-allergic reactions.^{4,5} Furthermore, the case report of Rial et al.,⁶ showed a decrease of food-allergic reaction to corn and nuts after accidental food ingestion during dupilumab treatment for AD, and provides clinical evidence for the positive effect of dupilumab in decreasing the severity of a food-allergic reaction. In our study, 33 of 40 patients, who accidentally ingested foods during dupilumab treatment, reported a decrease in severity of food-allergic symptoms ([Table S2](#)). However, studies including food challenges before and during dupilumab treatment are necessary to evaluate and objectify whether dupilumab is an effective treatment for FA.

We hypothesize that dupilumab might decrease the severity of food-allergic reactions due to inhibiting the IL-4/IL-13-pathway. IL-4 and IL-13 play a key role in differentiation of plasma cells from B lymphocytes, IgE class-switching and subsequently expansion, maintenance and activation of mast cells and basophils, causing the release of mediators leading to allergic symptoms.¹ Therefore, blocking the IL-4/IL-13 signaling pathway, by using dupilumab, might diminish food-allergic reactions by interfering in the food-allergic reaction cascade.

TABLE 1 Baseline characteristics

	Total
Total (n, %)	125 (100)
Gender (female), n (%)	58 (46.4)
Age, mean (SD) ^a	35.7 (12.5)
EASI score, mean (SD)	16.9 (9.0)
Number of food allergies, n (%)	
1	42 (33.6)
2	35 (28.0)
3	15 (12.0)
4	18 (14.4)
5	12 (9.6)
6	3 (2.4)
Food allergen, number and sIgE levels	
Peanut, n (%)	63 (51.2)
Extract (kU/L), median (IQR)	22.1 (4.5–51.0)
Ara h 2 (kU/L), median (IQR)	7.7 (1.3–34.2)
Ara h 8 (kU/L), median (IQR)	12.5 (2.8–25.8)
Hazelnut, n (%)	65 (52.0)
Extract (kU/L), median (IQR)	33.2 (16.5–62.0)
Cor a 1 (kU/L), median (IQR)	41.5 (17.7–73.0)
Cor a 9 (kU/L), median (IQR)	0.9 (0.1–4.4)
Cor a 14 (kU/L), median (IQR)	0.4 (0.2–2.1)
Almond, n (%)	30 (24.0)
Extract (kU/L), median (IQR)	3.3 (1.7–5.5)
Cashewnut, n (%)	30 (24.0)
Extract (kU/L), median (IQR)	12.4 (5.0–27.4)
Walnut, n (%)	36 (28.8)
Extract (kU/L), median (IQR)	10.4 (2.3–27.3)
Kiwi, n (%)	38 (30.4)
Extract (kU/L), median (IQR)	5.2 (1.5–11.1)
Apple, n (%)	44 (35.2)
Extract (kU/L), median (IQR)	12.9 (4.2–22.2)
Atopic comorbidity, n (%)	
Allergic Asthma	92 (73.6)
Allergic Rhinitis	102 (81.6)
Allergic Conjunctivitis	96 (76.8)
Laboratory findings	
Serum TARC levels, median (IQR)	2083 (1117.3–3696.3)
Eosinophils levels, median (IQR)	0.38 (0.18–0.63)

Note: Missing laboratory findings: serum TARC levels $n = 1$, eosinophils levels $n = 1$. Missing baseline sIgE: peanut $n = 2$, hazelnut $n = 3$, almond $n = 1$, walnut = 1, kiwi = 1.

Abbreviations: IQR, Interquartile range; SD, standard deviation; TARC, thymus and activation-regulated chemokine.

^aAge at dupilumab treatment initiation.

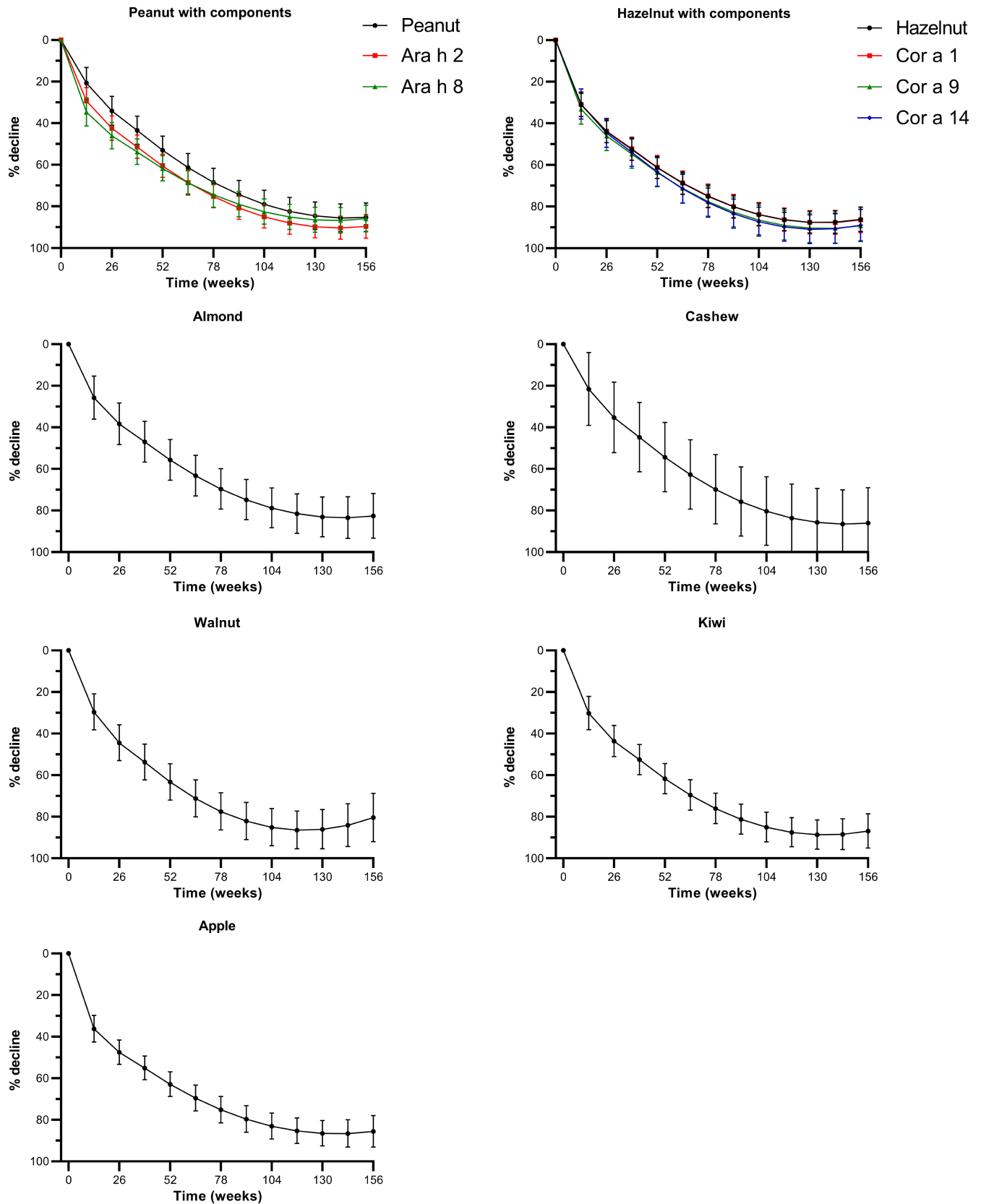


FIGURE 1 Estimated percentage decrease of sIgE levels during dupilumab treatment in patients with AD over the course of 3 years for peanut (incl. Ara h 2 and Ara h 8), hazelnut (incl. Cor a 1, Cor a 9 and Cor a 14), almond, cashew nut, walnut, kiwi, and apple. Error bars indicate the 95% confidence interval.

In conclusion, this daily practice study shows that dupilumab treatment induces a sustained decrease in sIgE levels, showing an estimated decrease of at least 80% for all foods after 3 years of treatment. These findings endorse a possible additional advantage of dupilumab for AD patients with concomitant food allergy.

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CONFLICT OF INTEREST

L. Spekhorst is a speaker for Abbvie. L. van der Rijst, N. Zuithoff, A. Knulst, and M. van Megen have nothing to disclose. M. de Graaf is an advisor, consultant, speaker or investigator for Sanofi-Genzyme, Regeneron Pharmaceuticals, LEO Pharma and Eli Lilly. M. de Bruin-Weller has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Arena, Aslan, Eli Lilly, Galderma, Janssen, Leo Pharma, Pfizer, Regeneron, and Sanofi-Genzyme. TM. Le has been an advisory board member for Novartis and speaker for Thermo Fisher Scientific.

Lotte S. Spekhorst¹ 

Lisa P. van der Rijst¹

Marlies de Graaf¹

Maxime van Megen¹

Nicolaas P. A. Zuithoff²

André C. Knulst¹

Marjolein S. de Bruin-Weller¹ 

Thuy-My Le¹

¹National Expertise Center for Atopic Dermatitis, Department of Dermatology and Allergology, University Medical Center Utrecht, Utrecht, The Netherlands

²Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

Correspondence

Lisa P. van der Rijst, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands.

Email: l.p.vanderrijst-3@umcutrecht.nl

Lotte S. Spekhorst, Lisa P. van der Rijst, Marjolein S. de Bruin-Weller and Thuy-My Le contributed equally.

ORCID

Lotte S. Spekhorst  <https://orcid.org/0000-0002-7537-765X>

Marjolein S. de Bruin-Weller  <https://orcid.org/0000-0002-1249-6993>

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.