Safety and Effectiveness of Dupilumab in the Treatment of Atopic Dermatitis in Japanese Patients: The First Interim Analysis Report From Post-Marketing Surveillance

Hiroyuki Fujita[1], Katsuhisa Suzuki[1], Kazuhiko Arima[1]

[1]Sanofi K.K., Tokyo, Japan

BACKGROUND

- Dupilumab blocks the shared receptor component for interleukin-4 and interleukin-13, key and central drivers of type 2 inflammation in multiple diseases[1]
- In Japan, dupilumab was approved in January 2018 for the treatment of atopic dermatitis (AD) in adults with inadequate responses to existing therapies[2]

OBJECTIVE

- **To evaluate the safety and effectiveness of dupilumab treatment in Japanese adults with AD in a real-world setting**

METHODS

Study

- This observational, multicenter post-marketing surveillance was conducted in patients who received dupilumab for the treatment of AD in Japan (UMIN-CTR Trials Registry: UMIN000032807)
- Practice is per real-world practice and therefore concomitant medications were allowed and none were prohibited
- Eligible patients
  - Patients who are newly treated with dupilumab and who have consented to participate in this study
- Study period: July 2018–June 2022 (planned)
- Enrollment period: July 2018–June 2020
- Observation period
  - Two years from the start of dupilumab treatment (regardless of whether the drug is discontinued)
- Dosing regimen
  - 600 mg of dupilumab administered subcutaneously as a loading dose, followed by 300 mg every other week per approved posology; concomitant medications were allowed

Outcomes

- Safety
  - Incidence of adverse drug reactions (ADR)
- Effectiveness
  - Mean Eczema Area and Severity Index (EASI) over time
  - Proportion of patients with ≥ 50%/75%/90% improvement in EASI (EASI-50/75/90) relative to pre-dupilumab treatment at baseline
  - Mean Peak Pruritus Numerical Rating Scale (NRS) scores over time
  - Mean Dermatology Life Quality Index (DLQI) over time
  - Mean absolute biomarker values over time
    - TARC (thymus and activation-regulated chemokine)
    - Peripheral blood eosinophil count
    - Total IgE
    - Lactate dehydrogenase (LDH)

METHODS (CONT.)

Analysis

- All analysis were carried out in the safety analysis set (all patients who received ≥ 1 dose of dupilumab) and the effectiveness analysis set (all patients who reported ≥ 1 effectiveness measurement in the safety analysis set)
- All analyses are descriptive and are based on the available measurements at a particular timepoint with no imputation for missing values (as observed)
- This analysis has a data cutoff of March 26, 2020 and the presented effectiveness data is from 4 months of follow-up (the safety data is based on fixed data as of March 26, 2020)

RESULTS

- At the time of this interim analysis, the duration of dupilumab treatment was 24.6 ± 14.5 weeks (mean ± SD)

Table 1. Baseline demographics and disease characteristics.

	Safety analysis set (N = 231)
Age,[a] n (%)	
< 15 years	0
≥ 15 to < 18 years	13 (5.6)
≥ 18 to < 65 years	197 (85.3)
≥ 65 years	21 (9.1)
Age at AD onset, n (%)	
< 6 years	83 (35.9)
≥ 6 to < 18 years	51 (22.1)
≥ 18 years	43 (18.6)
Unknown	54 (23.4)
Sex, n (%)	
Male	165 (71.4)
Female	66 (28.6)
Height, mean (± SD), cm	165.0 (± 8.1)
Weight, mean (± SD), kg	61.6 (± 12.1)
	Effectiveness analysis set
EASI, mean (± SD), n = 218	31.3 (± 13.7)
7-day average worst itch NRS score, mean (± SD), n = 100	7.0 (± 2.2)
DLQI, mean (± SD), n = 180	12.0 (± 6.4)
TARC, mean (± SD), pg/mL, n = 157	5046.4 (± 6158.0)
Peripheral blood eosinophil count, mean (± SD), eosinophils/mm^3, n = 150	842.9 (± 996.9)
Total IgE, mean (± SD), IU/mL, n = 151	10999.5 (± 13255.6)
LDH, mean (± SD), IU/L, n = 155	317.6 (± 147.5)

Of the 231 patients with a case report form collected, 38 discontinued dupilumab. The main reasons for discontinuation were improvement of the primary disease (9 cases), economic reasons (7 cases), occurrence of adverse events (3 cases), and insufficient clinical effect (2 cases).SD, standard deviation.
[a]In Japan, regulatory approved age is ≥ 15 years. Labeling posologies may differ outside Japan.

RESULTS (CONT.)

Table 2. Treatments for AD.

	Safety analysis set (N = 231)	
	Prior medication/ intervention[a]	Concomitant medication/intervention
Medications, n (%)		
Topical corticosteroid	201 (87.0)	202 (87.5)
Topical calcineurin inhibitor	100 (43.3)	113 (48.9)
Moisturizer	157 (68.0)	161 (69.7)
Oral corticosteroid	16 (6.9)	10 (4.3)
Oral non-steroidal immunosuppressant	27 (11.7)	14 (6.1)
Other	148 (64.1)	145 (62.8)
Interventions, n (%)		
Ultraviolet phototherapy	14 (6.1)	2 (0.9)
Hospitalization/hospital admission	10 (4.3)	1 (0.4)

Multiple options could be chosen, so percentages might not add up to 100%.
[a]This data was collected 3 months prior to enrollment.

Table 3. Safety assessment (reported ADRs).

n (%)	Safety analysis set (N = 231)
Proportion of patients with ≥ 1 ADR	44 (19.1)
Infections and parasitosis (SOC)	21 (9.1)
Conjunctivitis (PT)	21 (9.1)
Pyoderma (PT)	1 (0.4)
Nervous system disorder (SOC)	3 (1.3)
Dizziness (PT)	1 (0.4)
Headache (PT)	2 (0.9)
Eye disorder (SOC)	18 (7.8)
Blepharitis (PT)	3 (1.3)
Allergic conjunctivitis (PT)	13 (5.6)
Eye discharge (PT)	1 (0.4)
Eye pruritus (PT)	2 (0.9)
Gastrointestinal disorders (SOC)	1 (0.4)
Vomiting (PT)	1 (0.4)
Skin and subcutaneous tissue disorders (SOC)	3 (1.3)
Skin dryness (PT)	1 (0.4)
Erythema (PT)	1 (0.4)
Skin exfoliation (PT)	1 (0.4)
Nail ridging (PT)	1 (0.4)
General and systemic disorders and conditions at the site of administration (SOC)	1 (0.4)
Erythema at injection site (PT)	1 (0.4)
Injection site pruritus (PT)	1 (0.4)

ADRs encoded according to MedDRA-J version 22.1
MedDRA-J, Medical Dictionary for Regulatory Activities in Japanese; PT, MedDRA Preferred Term; SOC, MedDRA System Organ Class.

CONCLUSION

- **In this real-world setting, safety and effectiveness of dupilumab among Japanese adults with AD were similar to those observed in clinical trials**

Figure 1. Effectiveness: (A) EASI; (B) Proportion of patients achieving EASI-50/75/90 (C) Weekly average worst itch NRS score; (D) DLQI.

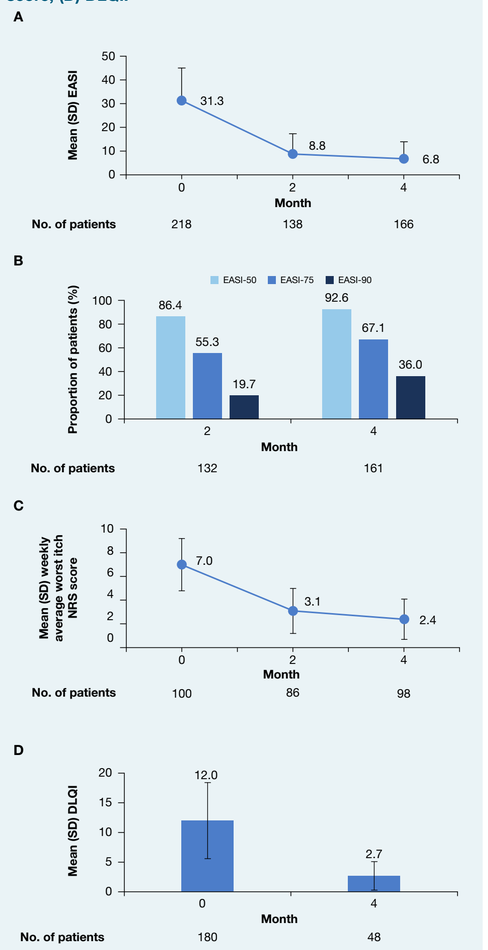
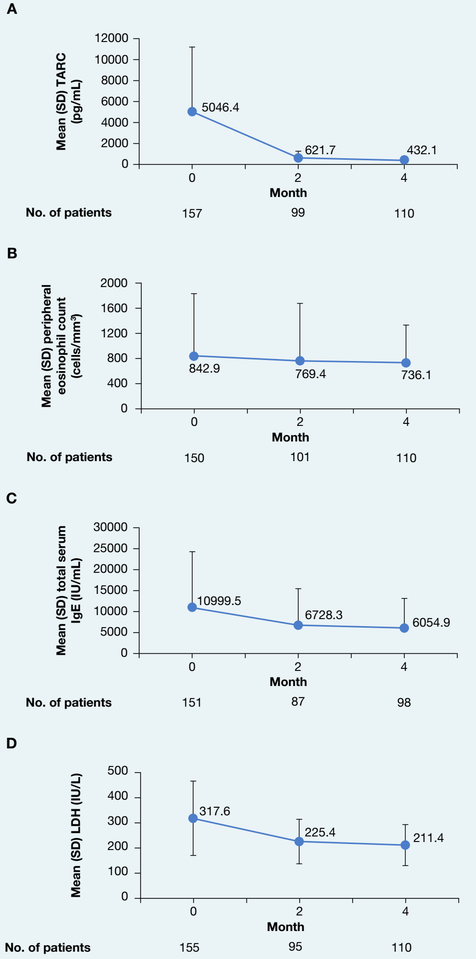


Figure 2. Biomarkers: (A) TARC; (B) Peripheral eosinophil counts; (C) Total serum IgE; (D) LDH.



References: 1. Gandhi et al. Nat Rev Drug Discov. 2016;15:35-50. 2. Miyano K, Tsunemi Y. Current treatments for atopic dermatitis in Japan. J Dermatol. 2021;48:140-51.

Acknowledgments: Data first presented at the 120th Annual Meeting of the Japanese Dermatology Association (JDA 2021); Virtual Meeting; June 10-13, 2021. Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov Identifiers: UMIN-CTR Trials Registry: UMIN000032807. Medical writing/editorial assistance was provided by Amy O'Callaghan, PhD, of Excerpta Medica, and was funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc., according to the Good Publication Practice guideline.

Disclosures: Fujita H, Suzuki K, Arima K: Sanofi K.K. – employees, may hold stock and/or stock options in the company.

Presented at the 3rd Annual Revolutionizing Atopic Dermatitis Conference (RAD 2021); Virtual Conference; December 11–13, 2021.