Allergy Asthma Immunol Res. 2024 Jul;16(4):372-386
https://doi.org/10.4168/aair.2024.16.4.372
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Original Article

Check for updates

Long-term Safety and Efficacy of Dupilumab in Patients With Uncontrolled, Moderate-to-Severe Asthma Recruited From Korean Centers: A Subgroup Analysis of the Phase 3 LIBERTY ASTHMA TRAVERSE Trial

Chin Kook Rhee [1], **Jung-Won Park** [2], **Heung-Woo Park** [3], **Hayeon Noh** [4], **Jerome Msihid** [5], **You Sook Cho** [6*]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea
[2]Division of Allergy and Immunology, Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul, Korea
[3]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea
[4]Sanofi Specialty Care Medical Korea, Sanofi, Seoul, Korea
[5]HEVA Analytics, Sanofi, Gentilly, France
[6]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Received: Dec 1, 2023
Revised: Feb 19, 2024
Accepted: Mar 6, 2024
Published online: May 17, 2024

Correspondence to
You Sook Cho, MD, PhD
Division of Allergy and Clinical Immunology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea.
Tel: +82-2-3010-3285
Fax: +82-2-3010-6969
Email: yscho@amc.seoul.kr

ORCID iDs
Chin Kook Rhee
https://orcid.org/0000-0003-4533-7937
Jung-Won Park
https://orcid.org/0000-0003-0249-8749
Heung-Woo Park
https://orcid.org/0000-0002-6970-3228
Hayeon Noh
https://orcid.org/0009-0005-1235-0571
Jerome Msihid
https://orcid.org/0000-0003-4733-5855
You Sook Cho
https://orcid.org/0000-0001-8767-2667

ABSTRACT

Purpose: Long-term data are limited on the safety and efficacy of dupilumab in patients with uncontrolled, moderate-to-severe asthma from Korea. The current subgroup analysis was designed to evaluate the long-term safety and efficacy of dupilumab in patients enrolled from Korean centers in the parent studies (phase 2b and QUEST) and who participated in the TRAVERSE open-label extension (OLE) study.
Methods: TRAVERSE was a global, multicenter, OLE study that assessed the safety and efficacy of dupilumab 300 mg every 2 weeks for up to 96 weeks in patients (n = 2,282) with uncontrolled, moderate-to-severe asthma who completed prior dupilumab asthma clinical trials. The primary outcome was the incidence of any treatment-emergent adverse events (TEAEs); the secondary outcomes included annualized severe exacerbation rate, pre-bronchodilator forced expiratory volume in 1 second (pre-BD FEV1), and 5-item Asthma Control Questionnaire (ACQ-5) score.
Results: Safety outcomes were consistent with the parent studies and the overall TRAVERSE population; out of 74 patients, 70 experienced ≥ 1 TEAE, and 6 (8.1%) discontinued because of adverse events. During the treatment period, the unadjusted annualized severe exacerbation rate was low (0.470). Improvement in pre-BD FEV1 was seen as early as Week 2 with a mean change from the parent study baseline (PSBL), standard deviation (SD) of 0.42 L (0.47), which was sustained until Week 96. Mean change from PSBL (SD) in ACQ-5 score was −1.32 (0.76) at Week 48.
Conclusions: This subgroup analysis of TRAVERSE showed the long-term safety and efficacy of dupilumab in patients with uncontrolled, moderate-to-severe asthma enrolled from Korean centers.

Allergy, Asthma & Immunology Research AAIR

Trial Registration
ClinicalTrials.gov Identifier: NCT02134028

Disclosure
Chin Kook Rhee, Heung-Woo Park, and You Sook Cho are on the advisory panel on Sanofi, Korea; Hayeon Noh and Jerome Msihid are employees of Sanofi and may hold stocks or stock options in the company. Heung-Woo Park serves as a deputy editor for the Allergy, Asthma & Immunology Research journal and recuses himself from the editorial decisions on this manuscript. Jung-Won Park and You Sook Cho serve as editorial board members for the Allergy, Asthma & Immunology Research journal and recuse themselves from the editorial decisions on this manuscript.

Data Availability Statement
Qualified researchers may request access to patient-level data and related study documents, including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan, and dataset specifications. Patient-level data will be anonymized, and study documents will be redacted to protect the privacy of the trial participants. Further details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at: https://www.vivli.org/.

Trial Registration: ClinicalTrials.gov Identifier: NCT02134028

Keywords: Dupilumab; clinical trial; phase III; safety; efficacy; Koreans; asthma

INTRODUCTION

Asthma is a common disease of the airways characterized by chronic inflammation and variable airflow obstruction.[1] Severe asthma is a subset of difficult-to-treat asthma that is uncontrolled despite adherence with maximal optimized therapy and treatment of contributory factors, or that worsens when high-dose treatment is decreased.[2,3] In Korea, the prevalence of severe asthma has increased from 3.5% (in 2002) to 6.1% (in 2015) among total asthmatics.[4,5] A large proportion of patients with severe asthma present with type 2 inflammation in the airways as an underlying pathology, and a subgroup of these patients may have persistent asthma symptoms despite treatment with corticosteroids; therefore, novel treatment strategies are needed.[6]

Dupilumab, a fully human monoclonal antibody that blocks interleukin 4 and interleukin 13 signaling pathways, key and central drivers of type 2 inflammation,[7] is approved in Korea as an add-on maintenance treatment for patients (≥ 12 years) with severe asthma characterized by blood eosinophil count ≥ 150 cells/μL or fractional exhaled nitric oxide ≥ 25 ppb or with oral corticosteroid (OCS) dependent asthma.[8] The efficacy and safety of dupilumab have been demonstrated in previous clinical trials, including phase 3 QUEST (NCT02414854), phase 2b study (NCT01854047), and phase 3 VENTURE (NCT02528214).[9-11] Dupilumab's long-term use is further supported by the phase 3 LIBERTY ASTHMA TRAVERSE open-label extension (OLE; NCT02134028),[12,13] which included adult and adolescent patients with moderate-to-severe asthma who participated in a prior dupilumab asthma clinical study, including phase 2a EXPEDITION (NCT02573233),[14] phase 2b,[15] phase 3 QUEST,[16] and phase 3 VENTURE studies.[11]

The current *post hoc* analysis of the TRAVERSE study was designed to evaluate the long-term safety and efficacy of dupilumab in a subgroup of patients from Korean centers who completed one of the parent studies and subsequently enrolled in the OLE.

MATERIALS AND METHODS

Study design and patients

TRAVERSE (NCT02134028) was a global, multicenter, OLE study that assessed the long-term safety and efficacy of dupilumab for up to 96 weeks in adult and adolescent patients (aged 12–84 years) with moderate-to-severe asthma.[12,13] The study protocol was approved by independent ethics committees and Institutional Review Boards at the respective study sites; the study was conducted in accordance with the Declaration of Helsinki and the Good Clinical Practice guidelines.[13] Informed consent was obtained from all the patients (or their representatives) before their enrolment in the study.[13]

Detailed study design, eligibility criteria, and trial outcomes of TRAVERSE were previously published.[13] In brief, the trial comprised a 0–3-week screening period, a 48–96-week treatment period (post protocol amendment, the treatment period was shortened from 96 weeks to 48 weeks), and a 12-week follow-up period. The trial included adult and adolescent

https://doi.org/10.4168/aair.2024.16.4.372

patients with moderate-to-severe asthma who completed prior dupilumab clinical trials, including phase 2b, phase 2a EXPEDITION, phase 3 QUEST, and phase 3 VENTURE studies. The only exception was that patients from the phase 2b study had to complete a 16-week follow-up period to enroll in TRAVERSE.

This subgroup analysis was performed in non-OCS-dependent patients recruited from Korean centers in QUEST and phase 2b study who enrolled in OLE; the other 2 studies (phase 2a EXPEDITION and VENTURE) did not enroll any patients from Korean centers and hence were excluded from this subgroup analysis. Irrespective of treatment (placebo [PBO] or dupilumab [DPL]) received in the parent studies, all patients in OLE received dupilumab 300 mg every 2 weeks subcutaneously throughout the treatment period. Patients continued background therapy (inhaled corticosteroid [ICS] + asthma controllers) as maintained during the parent studies.

Safety

The proportion of patients with treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (SAEs), or TEAEs leading to treatment discontinuation and death (if any) was assessed.

Anti-drug antibodies (ADAs) and neutralizing antibodies (NAbs)

The incidence of ADAs and NAbs and the effect of ADA and NAb response on the efficacy and safety of dupilumab were assessed. The presence of ADA in serum samples from patients was assessed using electro-chemiluminescence immunoassay that involved a 3-tier approach: an initial screen to identify samples that are potentially positive for ADA; a confirmation step to determine whether positive responses in the screen are specific for dupilumab; and a titer procedure to assess the level of ADA in confirmed positive samples. The presence of anti-dupilumab NAb in ADA-positive samples was assessed using a validated, competitive ligand binding assay that utilized dupilumab to capture NAb present in serum samples.

Efficacy

Previous studies have reported efficacy outcomes using unadjusted annualized severe exacerbation rate (AER) over the treatment period (the total number of events occurring during the treatment period divided by the total number of patient-years [PY] followed during the treatment period), change from parent study baseline (PSBL) in pre-bronchodilator forced expiratory volume in 1 second (pre-BD FEV1), asthma control as measured by the 5-item Asthma Control Questionnaire (ACQ-5, on a scale of 0–6, where higher scores represent lower asthma control), health-related quality of life as measured by the Asthma Quality of Life Questionnaire (AQLQ, on a scale of 0–7, where higher scores represent less impairment), and inflammatory biomarkers including blood eosinophils and total serum immunoglobulin E (IgE).[13,17] Because of a protocol amendment based on cumulative experience with dupilumab, the study was shortened from 96 weeks to 48 weeks, and ACQ-5 and AQLQ endpoints are thus reported up to Week 48. The analysis of serum IgE was conducted only for the patients from the phase 2b study because of changes in the protocol.

Statistical analysis

All analyses were *post hoc* and descriptive and were performed on a safety population, defined as all patients who received ≥ 1 dose or part dose of dupilumab. The comparator value for efficacy was the PSBL value.

https://doi.org/10.4168/aair.2024.16.4.372

All patients received dupilumab in the TRAVERSE study. Treatment in patients who received a placebo in the parent study and were exposed to dupilumab in TRAVERSE is referred to as PBO/DPL, while treatment in patients who received dupilumab in both studies is referred to as DPL/DPL. Safety and efficacy outcomes were presented for all 4 individual treatment groups (PBO/DPL [phase 2b study], DPL/DPL [phase 2b study], PBO/DPL [QUEST], and DPL/DPL [QUEST]) and the overall group (combined group of patients from all the 4 groups). Safety observations were reported in terms of the number (%) of patients with TEAEs, incidence rate based on PY, and the number of patients with ≥ 1 TEAE per 100 PY. Safety data were classified by system organ class and preferred term according to the Medical Dictionary for Regulatory Activities, version 22.0. Incidence of ADAs and NAbs was described in terms of the percentage of patients with treatment-emergent response, defined as a positive response in the ADA assay post first dose in TRAVERSE, when the baseline status in the parent study is negative or missing; the percentage of patients with a persistent response, defined as a treatment-emergent ADA-positive response with 2 or more consecutive ADA-positive sampling time points separated by > 12-week period (greater than 84 days), with no ADA-negative sample in between; the percentage of patients with a transient response is defined as a treatment-emergent ADA-positive response that is not considered persistent or indeterminate; the percentage of patients with indeterminate response, defined as a treatment-emergent response with only the last collected sample positive in the ADA assay; the percentage of patients with a treatment-boosted response, defined as a positive response in the ADA assay post first dose in the current study that is greater than or equal to 4-fold of the baseline titer levels of the parent studies, when baseline status of the parent studies are positive. Peak post-baseline titer values were also reported.

For efficacy outcomes, pre-BD FEV1, ACQ-5, and AQLQ scores were reported in terms of mean change from PSBL, mean and standard deviation (SD), median (95% confidence interval [CI]), and first and third quartiles (Q1 and Q3, respectively) values. A responder analysis was also performed on ACQ-5 and AQLQ scores; the proportion of patients who showed improvements from the PSBL exceeding the minimal clinically important difference of ≥ 0.5[18] were reported as responders. No imputations were made for patients with missing data.

All statistical analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Demographics and clinical characteristics of patients

Of 2,282 patients with moderate-to-severe asthma enrolled in the TRAVERSE OLE study, 1,530 were enrolled from the phase 3 QUEST study, and 532 were enrolled from the phase 2b study (**Fig. 1**). From Korean centers, 28 patients were recruited in the phase 2b study and 74 patients in the QUEST. Of them, 21/28 (75%) patients from the phase 2b study (n = 4 [PBO/DPL]; n = 17 [DPL/DPL]) and 53/74 (72%) from the QUEST study (n = 19 [PBO/DPL]; n = 34 [DPL/DPL]) were enrolled in the OLE study and were included in this analysis. Out of 74 patients included in this analysis, 66 (89.2%) completed OLE, and 8 (10.8%) discontinued it (6 because of adverse events and 2 for other reasons). The median (minimum–maximum) follow-up duration was 753.5 (111–1,244) days.

At PSBL, the mean ± SD age of the patients included in this subgroup analysis was 53.60 ± 10.50 years (**Table 1**). ACQ-5 and AQLQ scores showed that patients had inadequate asthma

https://doi.org/10.4168/aair.2024.16.4.372

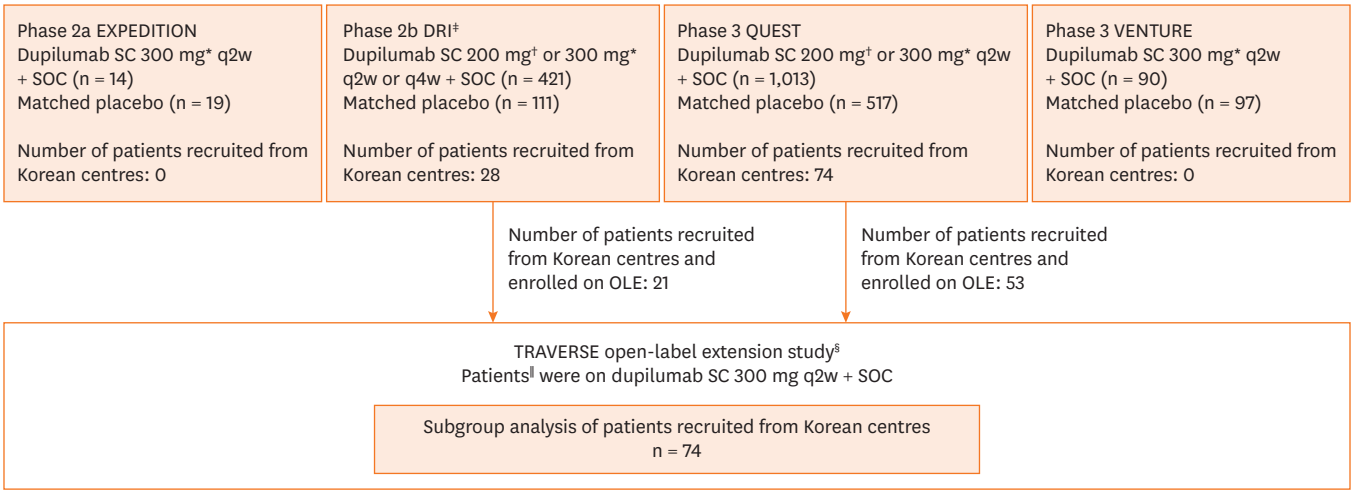


Fig. 1. Study design of Korean subgroup analysis of the phase 3 LIBERTY ASTHMA TRAVERSE trial. Patient numbers presented for parent studies represent the number of patients who enrolled in and were exposed to treatment in the OLE.
SC, subcutaneous; SOC, standard of care; q2w, every 2 weeks; q4w, every 4 weeks; DRI, dose-ranging study; OLE, open-label extension.
*With 600 mg loading dose; †With 400 mg loading dose.
‡Eligible patients completed the 16-week post-treatment follow-up period of the parent study before being rolled over into TRAVERSE.
§Because of a protocol amendment based on cumulative experience with dupilumab, the study was shortened from 96 weeks to 48 weeks.
‖The 2,282 subjects enrolled in and exposed to treatment in OLE and 1,906 patients continued to be exposed to treatment beyond 48 weeks.

control and impaired quality of life, respectively. A total of 64 (86.5%) patients had ongoing atopic medical conditions. Most demographic and clinical characteristics were similar across patients from both the studies, except for FEV1 reversibility, which was higher in the PBO/DPL from phase 2b study vs. other groups, and the high-dose ICSs use, which was reported in a higher proportion of patients in the DPL/DPL from phase 2b study vs. other groups.

All patients included in the current analysis belong to Asian race and non-Hispanic ethnicity, compared with 12.4% of patients in the overall TRAVERSE population. In the current analysis, the age at the onset of asthma was higher, and the number of severe asthma exacerbations requiring hospitalization or urgent medical care during 1 year prior to the parent study was lower than in the overall TRAVERSE population (**Table 1**).

Safety

Among the 74 patients included in this analysis, 70 (94.6%) patients experienced ≥ 1 TEAE, with 14.9% reporting a treatment-emergent SAE (**Table 2**). The most frequently reported TEAEs were upper respiratory tract infection (43.2%), nasopharyngitis (12.2%), and injection site erythema (13.5%). The frequency of eosinophilia was low (2 [2.7%] patients), and no clinical events were associated with it. Both these events were resolved (one patient received oral prednisolone, and the other received no corrective treatment) and were assessed by the investigators as not related to dupilumab.

The incidence of treatment-emergent SAEs was number/total number (%): 1/4 (25%) and 1/17 (5.9%) in the PBO/DPL and DPL/DPL treatment groups from the phase 2b, and 2/19 (10.5%) and 7/34 (20.6%) from the QUEST. Musculoskeletal and connective tissue disorders and injury, poisoning, and procedural complications were found to be the most frequent treatment-emergent SAEs (**Supplementary Table S1**).

https://doi.org/10.4168/aair.2024.16.4.372

Table 1. Demographics and clinical characteristics of patients at PSBL—exposed patients from phase 2b study and QUEST who were recruited from Korean centers and enrolled in TRAVERSE

Characteristics	Patients from phase 2b study		Patients from QUEST		Overall Korean Subgroup (n = 74)	Overall TRAVERSE population* (n = 2,062)
	PBO/DPL (n = 4)	DPL/DPL (n = 17)	PBO/DPL (n = 19)	DPL/DPL (n = 34)		
Age (yr)	52.0 ± 16.9	54.4 ± 9.3	56.7 ± 9.4	51.7 ± 10.9	53.6 ± 10.5	48.4 ± 14.5
	53.0 (33.0–69.0)	55.0 (39.0–71.0)	57.0 (40.0–71.0)	52.0 (28.0–70.0)	54.5 (28.0–71.0)	50.0 (12.0–84.0)
Female, No. (%)	2 (50.0)	8 (47.0)	13 (68.0)	21 (62.0)	44 (60.0)	1,281 (62.0)
Race, No. (%)						
Asian	4 (100.0)	17 (100.0)	19 (100.0)	34 (100.0)	74 (100.0)	255 (12.0)
Ethnicity, No. (%)						
Not Hispanic	4 (100.0)	17 (100.0)	19 (100.0)	34 (100.0)	74 (100.0)	1,545 (74.9)
Hispanic	-	-	-	-	-	517 (25.1)
Age at onset of asthma (yr)	46.3 ± 13.9	41.9 ± 12.1	42.4 ± 13.0	39.8 ± 11.4	41.3 ± 12.0	27.5 ± 18.7†
	47.0 (30.0–61.0)	43.0 (15.0–63.0)	46.0 (15.0–61.0)	42.5 (16.0–59.0)	43.0 (15.0–63.0)	28.0 (0.0–77.0)†
Time since the first diagnosis of asthma (yr)	5.9 ± 3.4	12.4 ± 7.7	14.3 ± 9.7	12.0 ± 7.1	12.4 ± 7.9	21.0 ± 15.3†
	5.8 (2.8–9.3)	11.0 (1.2–30.1)	14.2 (1.2–34.2)	11.8 (1.4–37.3)	11.0 (1.2–37.3)	16.9 (1.1–76.1)†
With ongoing atopic medical condition‡, No. (%)	4 (100.0)	17 (100.0)	15 (78.9)	28 (82.4)	64 (86.5)	1,686 (81.8)†
Atopic dermatitis	1 (25.0)	2 (11.8)	0	1 (2.9)	4 (5.4)	203 (9.9)§
Allergic conjunctivitis	2 (50.0)	0	2 (10.5)	4 (11.8)	8 (10.8)	285 (13.9)‖
Allergic rhinitis	4 (100.0)	14 (82.4)	13 (68.4)	25 (73.5)	56 (75.7)	1,364 (66.5)‖
Chronic rhinosinusitis	0	5 (29.4)	10 (52.6)	14 (41.2)	29 (39.2)	369 (18.0)§
Nasal polyposis	0	3 (17.6)	3 (15.8)	9 (26.5)	15 (20.3)	265 (12.9)‖
Eosinophilic esophagitis	0	0	0	0	0	4 (0.2)‖
Food allergy	0	3 (17.6)	2 (10.5)	2 (5.9)	7 (9.5)	156 (7.6)‖
Hives	0	0	0	1 (2.9)	1 (1.4)	102 (5.0)§
Baseline total IgE ≥ 100 IU/mL and at least one baseline aeroantigen specific IgE is positive (≥ 0.35 IU/mL)	1 (25.0)	8 (47.1)	9 (47.4)	16 (47.1)	34 (45.9)	1,082 (53.0)¶
No. of severe asthma exacerbations# experienced in 1 yr prior to the parent study	1.5 ± 0.6	2.5 ± 1.9	2.4 ± 1.4	2.1 ± 1.1	2.2 ± 1.4	2.2 ± 2.1
	1.5 (1.0–2.0)	2.0 (1.0–7.0)	2.0 (1.0–6.0)	2.0 (1.0–5.0)	2.0 (1.0–7.0)	2.0 (1.0–24.0)
No. of severe asthma exacerbations# requiring hospitalization or urgent medical care experienced in 1 yr prior to the parent study	0.0 ± 0.0	0.3 ± 0.6	0.4 ± 0.8	0.2 ± 0.5	0.3 ± 0.6	0.7 ± 1.4
	0.0 (0.0–0.0)	0.0 (0.0–2.0)	0.0 (0.0–3.0)	0.0 (0.0–2.0)	0.0 (0.0–3.0)	0.0 (0.0–18.0)
Pre-BD FEV1 (L)	1.7 ± 0.6	1.6 ± 0.3	1.3 ± 0.3	1.5 ± 0.5	1.5 ± 0.4	1.8 ± 0.6
	1.8 (1.1–2.2)	1.7 (1.2–2.2)	1.3 (0.9–2.0)	1.5 (0.7–2.8)	1.5 (0.7–2.8)	1.7 (0.4–4.2)
Pre-BD FEV1 per cent predicted (%)	67.3 (6.2)	65.4 (10.0)	58.1 (12.9)	60.1 (12.0)	61.2 (11.8)	59.0 (12.9)
	67.0 (60.0–75.0)	66.0 (44.0–80.0)	62.0 (37.0–75.0)	63.0 (30.0–79.0)	63.0 (30.0–80.0)	61.0 (13.0–99.0)
FEV1 reversibility (%)	44.2 ± 25.6	26.2 ± 15.9	25.7 ± 13.5	21.5 ± 16.1	24.9 ± 16.5	26.4 ± 20.3
	43.8	17.5	24.1	16.7	19.6	22.0
	(15.2–74.2)	(12.5–60.6)	(−3.1–56.7)	(2.8–61.1)	(−3.1–74.2)	(−37.3–268.9)
ACQ-5 score	2.4 ± 0.7	2.2 ± 0.4	2.3 ± 0.4	2.3 ± 0.6	2.3 ± 0.5	2.7 ± 0.8
	2.1 (1.8–3.4)	2.2 (1.6–3.0)	2.2 (1.8–3.2)	2.2 (0.6–4.0)	2.2 (0.6–4.0)	2.6 (0.0–6.0)
AQLQ global score	4.0 ± 1.4	3.7 ± 0.9	4.6 ± 0.7	4.8 ± 1.1	4.5 ± 1.1	4.2 ± 1.1
	4.5 (2.0–5.1)	3.8 (2.1–5.1)	4.4 (3.5–6.1)	4.9 (2.5–6.8)	4.4 (2.0–6.8)	4.2 (1.0–7.0)
High ICS dose, No. (%)	2 (50.0)	13 (77.0)	7 (37.0)	9 (27.0)	31 (42.0)	1,117 (54.5)§
Biomarkers, median (Q1–Q3)						
Blood eosinophil (G/L)	0.2 (0.1–0.5)	0.3 (0.2–0.4)	0.4 (0.1–1.1)	0.3 (0.1–0.7)	0.3 (0.1–0.7)	0.3 (0.1–0.5)
Total IgE (IU/mL)	412.0	154.0	140.0	195.0	173.0	180.0
	(33.5–1,552.5)	(84.0–410.0)	(75.0–350.0)	(96.0–379.0)	(75.0–410.0)	(66.0–447.5)
FeNO (ppb)	41.0 (31.5–69.0)	49.0 (34.0–66.0)	34.0 (21.0–69.0)	39.0 (19.0–59.0)	40.0 (23.0–61.0)	26.0 (15.0–45.0)

Data are presented as mean ± standard deviation in the first row and median (range) in the second row for each parameter, unless specified otherwise.
PSBL, parent study baseline; PBO, placebo; DPL, dupilumab; IgE, immunoglobulin E; pre-BD FEV1, pre-bronchodilator forced expiratory volume in 1 second; FEV1, forced expiratory volume in 1 second; ACQ-5, 5-item Asthma Control Questionnaire; AQLQ, Asthma Quality of Life Questionnaire (Standardized); ICS, inhaled corticosteroid; Q, quartile; FeNO, fractional exhaled nitric oxide; ppb, parts per billion.
*Rolled over from phase 2b and QUEST studies; †n = 2,060; §n = 2,049; ‖n = 2,050; ¶n = 2,043.
‡A patient is considered with an atopic medical history or ongoing atopic disease if the patient had or has any of the following diseases: atopic dermatitis, allergic conjunctivitis or allergic rhinitis, chronic rhinosinusitis, nasal polyposis, food allergy, history or baseline total IgE ≥ 100 IU/mL and at least one aeroantigen specific IgE ≥ 0.35 kUA/L at baseline.
#Asthma exacerbation prior to the study is defined as any treatment with one systemic (oral or parenteral) steroid burst or more for worsening asthma or hospitalization or an emergency/urgent medical care visit for worsening asthma.

https://doi.org/10.4168/aair.2024.16.4.372

Table 2. Summary of TEAEs—exposed patients from phase 2b and QUEST who were recruited from Korean centers and rolled over into TRAVERSE

TEAEs	Patients from phase 2b study*		Patients from QUEST		Overall
	PBO/DPL (n = 4, PY = 8.3)	DPL/DPL (n = 17, PY = 35.2)	PBO/DPL (n = 19, PY = 26.3)	DPL/DPL (n = 34, PY = 49.1)	(n = 74, PY = 118.9)
Category, No. (%)					
Patients with any TEAE	3 (75.0)	17 (100)	18 (94.7)	32 (94.1)	70 (94.6)
Patients with any treatment-emergent SAE	1 (25.0)	1 (5.9)	2 (10.5)	7 (20.6)	11 (14.9)
Patients with any TEAE leading to death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with any TEAE leading to permanent treatment discontinuation	0 (0.0)	0 (0.0)	1 (5.3)	5 (14.7)	6 (8.1)
No. of patients with any TEAE (PT ≥ 2% in any treatment group), No. (%), nP/PY (nP/100 PY)					
Upper respiratory tract infection	3 (75.0)	7 (41.2)	10 (52.6)	12 (35.3)	32 (43.2)
	3/4.0 (75.2)	7/24.5 (28.6)	10/18.8 (53.1)	12/31.2 (38.5)	32/78.5 (40.8)
Nasopharyngitis	0 (0.0)	2 (11.8)	1 (5.3)	6 (17.6)	9 (12.2)
	0/8.3	2/32.8 (6.1)	1/25.5 (3.9)	6/44.2 (13.6)	9/110.8 (8.1)
Bronchitis	0 (0.0)	0 (0.0)	1 (5.3)	2 (5.9)	3 (4.1)
	0/8.3	0/35.2	1/25.7 (3.9)	2/47.5 (4.2)	3/116.8 (2.6)
Herpes zoster	0 (0.0)	2 (11.8)	0 (0.0)	1 (2.9)	3 (4.1)
	0/8.3	2/33.0 (6.1)	0/26.3	1/48.7 (2.1)	3/116.4 (2.6)
Pharyngitis	1 (25.0)	0 (0.0)	1 (5.3)	1 (2.9)	3 (4.1)
	1/6.4 (15.6)	0/35.2	1/25.5 (3.9)	1/47.8 (2.1)	3/115.0 (2.6)
Periodontitis	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)	1 (1.4)
	0/8.3	0/35.2	0/26.3	1/47.0 (2.1)	1/116.9 (0.9)
Neutropenia	0 (0.0)	0 (0.0)	1 (5.3)	2 (5.9)	3 (4.1)
	0/8.3	0/35.2	1/25.6 (3.9)	2/47.7 (4.2)	3/116.9 (2.6)
Eosinophilia†	0 (0.0)	1 (5.9)	1 (5.3)	0 (0.0)	2 (2.7)
	0/8.3	1/34.1 (2.9)	1/24.3 (4.1)	0/49.1	2/115.8 (1.7)
Headache	1 (25.0)	1 (5.9)	0 (0.0)	4 (11.8)	6 (8.1)
	1/7.9 (12.7)	1/33.4 (3.0)	0/26.3	4/46.7 (8.6)	6/114.3 (5.3)
Oropharyngeal pain	0 (0.0)	1 (5.9)	2 (10.5)	2 (5.9)	5 (6.8)
	0/8.3	1/33.6 (3.0)	2/24.5 (8.2)	2/46.7 (4.3)	5/113.1 (4.4)
Productive cough	0 (0.0)	2 (11.8)	0 (0.0)	2 (5.9)	4 (5.4)
	0/8.3	2/32.8 (6.1)	0/26.3	2/46.9 (4.3)	4/114.3 (3.5)
Diarrhoea	0 (0.0)	1 (5.9)	0 (0.0)	2 (5.9)	3 (4.1)
	0/8.3	1/33.3 (3.0)	0/26.3	2/47.7 (4.2)	3/115.6 (2.6)
Nausea	0 (0.0)	1 (5.9)	2 (10.5)	0	3 (4.1)
	0/8.3	1/33.2 (3.0)	2/23.8 (8.4)	0/49.1	3/114.3 (2.6)
Eczema	1 (25.0)	0	0	0	1 (1.4)
	1/8.3 (12.0)	0/35.2	0/26.3	0/49.1	1/118.9 (0.8)
Arthralgia	2 (50.0)	1 (5.9)	1 (5.3)	1 (2.9)	5 (6.8)
	2/6.0 (33.5)	1/33.3 (3.0)	1/25.4 (3.9)	1/49.0 (2.0)	5/113.8 (4.4)
Back pain	1 (25.0)	1 (5.9)	1 (5.3)	2 (5.9)	5 (6.8)
	1/6.3 (16.0)	1/35.2 (2.8)	1/25.4 (3.9)	2/46.3 (4.3)	5/113.1 (4.4)
Injection site erythema	1 (25.0)	1 (5.9)	3 (15.8)	5 (14.7)	10 (13.5)
	1/6.2 (16.0)	1/33.2 (3.0)	3/22.8 (13.2)	5/41.5 (12.0)	10/103.7 (9.6)
Injection site pruritus	0 (0.0)	1 (5.9)	1 (5.3)	1 (2.9)	3 (4.1)
	0/8.3	1/33.2 (3.0)	1/24.3 (4.1)	1/47.0 (2.1)	3/112.8 (2.7)
Injection site pain	0 (0.0)	1 (5.9)	0	0	1 (1.4)
	0/8.3	1/33.2 (3.0)	0/26.3	0/49.1	1/116.9 (0.9)
Blood creatine phosphokinase increased	0 (0.0)	0	1 (5.3)	1 (2.9)	2 (2.7)
	0/8.3	0/35.2	1/24.4 (4.1)	1/47.5 (2.1)	2/115.5 (1.7)

TEAE, treatment-emergent adverse event; PBO, placebo; DPL, dupilumab; PY, patient-years; nP, number of patients with any event; nP/100 PY, number of patients with at least one event per 100 patient-years; PT, preferred term; SAE, serious adverse event.
*For the patients from the phase 2b study, there was a gap (≥ 16 weeks) between the last dose in the phase 2b study and the first dose in TRAVERSE, because the patients needed to complete the 16-week follow-up of phase 2b study to enroll in TRAVERSE; †Blood eosinophils > 3,000 cells/μL.

Overall, 6 (8.1%) patients (all from QUEST) discontinued the treatment because of a TEAE, with skin and subcutaneous tissue disorders being the most frequent events leading to discontinuation (**Supplementary Table S1**). No TEAE led to death in any of the treatment groups.

https://doi.org/10.4168/aair.2024.16.4.372

ADAs and NAbs

A total of 7 patients (2 patients from the phase 2b study and 5 patients from the QUEST) showed treatment-emergent ADA response (**Supplementary Table S2**). Persistent response was observed in 2 patients. Transient response was observed in 4 patients, and indeterminate response was observed in 1 patient. No treatment-boosted responses were observed. All 7 responses showed a low ADA titer value (< 1,000) with an overall median (interquartile range) peak post-baseline ADA titer of 120.0 (30.0–120.0).

A total of 3 patients showed a positive NAb status with a low-titer response (< 1,000; **Supplementary Table S3**). Among these patients, one showed no improvement in lung function (an FEV1 of 1.08 L at PSBL and that of 1.02 L at Week 48) during the treatment period. The other 2 patients showed moderate improvement (FEV1 increased from 1.27 L at PSBL to 1.85 L at week 48 in one patient and from 1.88 L to 2.09 L in the other).

Efficacy

Exacerbation rates

Reductions in the severe asthma exacerbations observed with dupilumab in the parent studies[9,10] were sustained in TRAVERSE. At PSBL, the mean ± SD number of severe exacerbations experienced in the 1 year prior to the parent study in patients enrolled from Korea was 2.24 ± 1.39 in the overall group (combined group of patients from all the 4 groups). Unadjusted AER was 0.000 (PBO) and 0.128 (combined DPL) from the phase 2b and 2.739 (combined PBO) and 0.384 (combined DPL) from theQUEST during the treatment period of the parent study.

In total, 51 (68.9%) of patients experienced no exacerbations during TRAVERSE, whereas 23 (31.1%) patients showed ≥ 1 severe exacerbation event with a total of 48 severe exacerbation events. Unadjusted AER was 0.470 in the overall group, 0.406 (PBO/DPL) and 0.255 (DPL/DPL) from the phase 2b, and 0.725 (PBO/DPL) and 0.507 (DPL/DPL) from the QUEST during TRAVERSE (**Fig. 2A**).

Lung function

Improvements in FEV1 observed with dupilumab in the parent studies[9,10] were maintained in the TRAVERSE. At PSBL, mean ± SD pre-BD FEV1 was 1.51 ± 0.44 L. Increase in pre-BD FEV1 was observed as early as week 2 with mean ± SD change from PSBL of 0.42 ± 0.47 L, which was maintained throughout the OLE period (**Fig. 2B**).

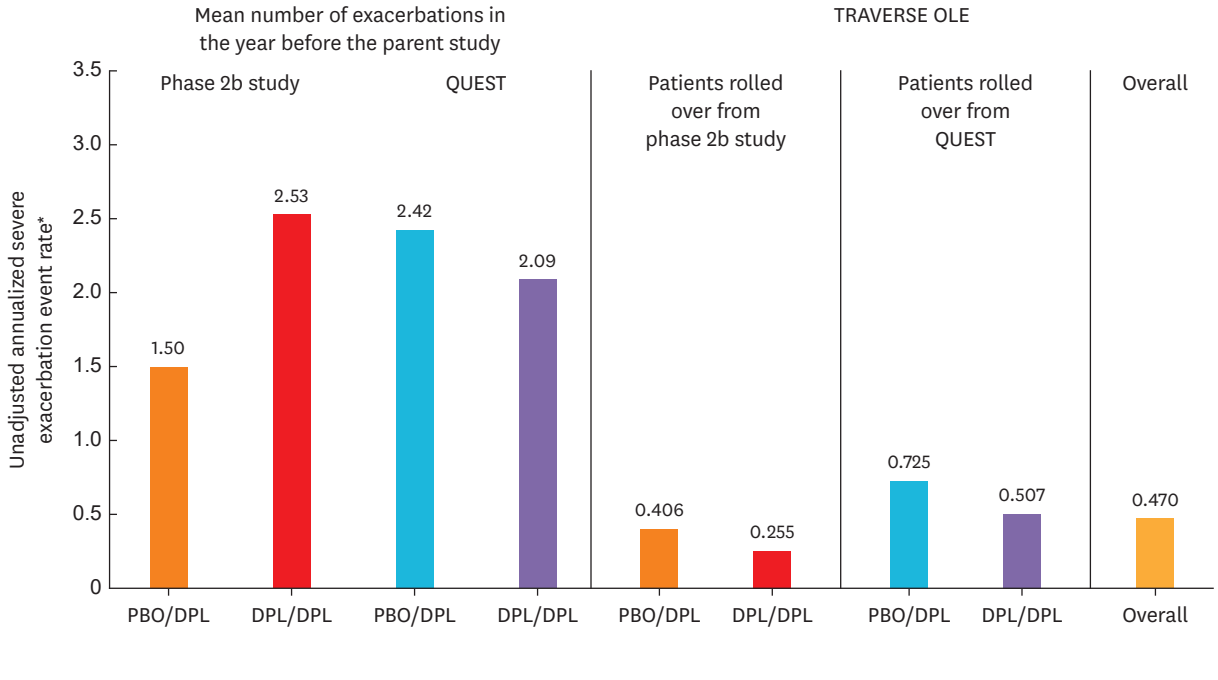
At PSBL, the pre-BD FEV1 (mean ± SD) was 1.71 ± 0.55 L (PBO/DPL) and 1.64 ± 0.30 L (DPL/DPL) from the phase 2b and was 1.33 ± 0.32 L (PBO/DPL) and 1.53 ± 0.52 L (DPL/DPL) from the QUEST. By week 96, the pre-BD FEV1 change (mean ± SD) from PSBL was 0.39 ± 0.14 L (PBO/DPL) and 0.33 ± 0.34 L (DPL/DPL) from the phase 2b and was 0.80 ± 0.32 L (PBO/DPL) and 0.51 ± 0.52 L (DPL/DPL) from the QUEST (**Fig. 2B**).

In the PBO/DPL group of the QUEST study, a sudden increase in FEV1 was observed at week 72, which could be due to a drop in the number of patients from 17 at week 48 to 6 at week 72 (**Fig. 2B**).

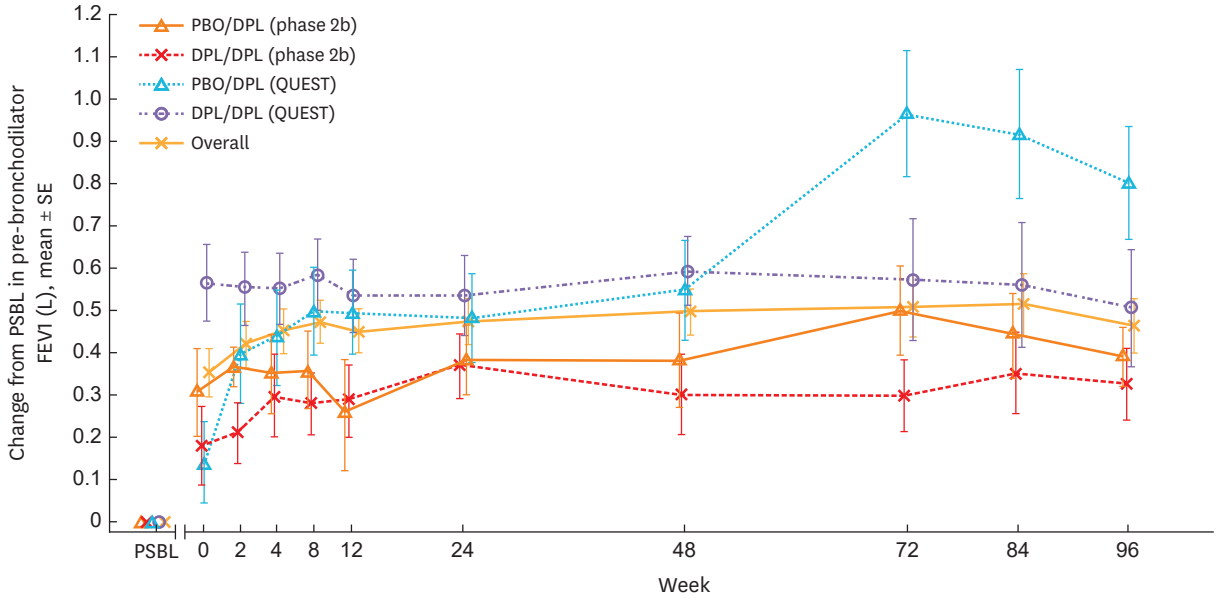
Asthma control and health-related quality of life

Improvements in asthma control observed with dupilumab during the parent studies[9,10]were sustained in the TRAVERSE. At PSBL, the mean ± SD ACQ-5 score was 2.28 ± 0.53 in the

https://doi.org/10.4168/aair.2024.16.4.372



A



No. of patients											
PBO/DPL (phase 2b)	4	4	4	4	4	4	4	4	4	4	4
DPL/DPL (phase 2b)	17	17	17	17	17	16	17	17	17	17	17
PBO/DPL (QUEST)	19	19	19	18	18	18	18	17	6	6	6
DPL/DPL (QUEST)	34	34	33	34	30	32	31	30	14	14	14
Overall	74	74	73	73	69	70	70	68	41	41	41

B

Fig. 2. Exacerbation rates and lung function in exposed patients from phase 2b and QUEST who were recruited from Korean centers and enrolled in TRAVERSE. (A) Annualized event rate of severe exacerbation during the treatment period and (B) mean change from PSBL in pre-bronchodilator FEV1 (L) over time. For the patients from the phase 2b study, there was a gap (≥ 16 weeks) between the last dose in the phase 2b study and the first dose in TRAVERSE, because the patients needed to complete the 16-week follow-up of phase 2b study to enroll in TRAVERSE.
DPL, dupilumab; FEV1, forced expiratory volume in 1 second; OLE, open-label extension; PBO, placebo; PSBL, parent study baseline; SE, standard error.
*The total number of events that occurred during the treatment period divided by the total number of patient-years followed in the treatment period.

https://doi.org/10.4168/aair.2024.16.4.372

overall group, which decreased to 0.90 ± 0.91 at week 24 and 0.96 ± 0.87 at week 48. The mean change of ACQ-5 scores from PSBL ± SD in individual treatment groups is presented in **Fig. 3A**. At week 0 of OLE, there were 3/4 (75%) and 10/17 (58.8%) responders (i.e., an improvement from PSBL of ≥ 0.5) in PBO/DPL and DPL/DPL from the phase 2b, respectively, and 14/19 (73.7%) and 26/31 (83.9%) responders in PBO/DPL and DPL/DPL from the QUEST, respectively. At week 48, there were 3/4 (75%) and 12/17 (70.6%) responders in PBO/DPL and DPL/DPL from phase 2b, respectively, and 16/17 (94.1%) and 24/30 (80.0%) responders in PBO/DPL and DPL/DPL from QUEST, respectively (**Supplementary Table S4**).

Improvements in AQLQ global score seen with dupilumab in the parent studies[9,10] were sustained during TRAVERSE. At PSBL, the mean ± SD AQLQ score was 4.46 ± 1.09 in the overall group, which increased to 5.38 ± 1.07 at wweek 24 and 5.37 ± 1.11 at week 48 in the TRAVERSE. The mean change from PSBL ± SD AQLQ scores in individual treatment groups is presented in **Fig. 3B**. At week 0 of OLE, there were 3/4 (75%) and 9/16 (56.3%) responders (i.e., an improvement from PSBL of ≥ 0.5) in PBO/DPL and DPL/DPL from phase 2b, respectively, and 10/17 (58.8%) and 19/33 (57.6%) responders in PBO/DPL and DPL/DPL from QUEST, respectively. At week 48, there were 3/4 (75%) and 12/17 (70.6%) responders in PBO/DPL and DPL/DPL from phase 2b, respectively, and 10/15 (66.7%) and 17/29 (58.6%) responders in PBL/DPL and DPL/DPL from QUEST, respectively, demonstrating an increase in the number of responders to treatment over time (**Supplementary Table S4**).

Inflammatory biomarkers

At PSBL, the median (95% CI) blood eosinophil level was 0.310 G/L (0.180–0.390) in the overall group, which decreased during OLE to 0.145 G/L (0.110–0.190) at week 48 and 0.150 G/L (0.120–0.250) at week 96 (**Fig. 4A**). Median (95% CI) blood eosinophil levels in individual treatment groups are presented in **Fig. 4A**. In the PBO/DPL group of QUEST study, the upper CI value was relatively higher at week 72 than at other time points, which could be due to a drop in the number of patients from 17 at Week 48 to 6 at Week 72.

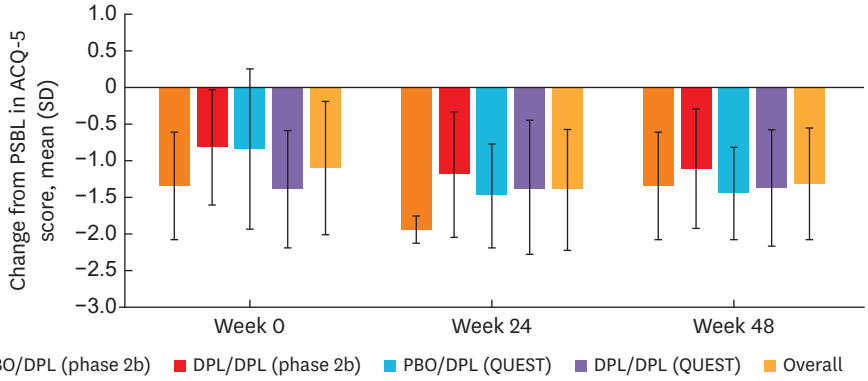
At PSBL, the median (95% CI) total IgE level was 154.0 (70.0–485.0) IU/mL in patients from the phase 2b study, which decreased during OLE to 25.0 (15.0–70.0) IU/mL at week 48 and 22.0 (12.0–52.0) IU/mL at week 96 (**Fig. 4B**). Median (95% CI) total IgE levels in individual treatment groups of the phase 2b study are presented in **Fig. 4B**. Total IgE levels were higher in the PBO/DPL group than in the DPL/DPL group at all time points; however, the levels were below PSBL levels.

DISCUSSION

This *post hoc* analysis showed that treatment with dupilumab 300 mg every 2 weeks was well tolerated and resulted in sustained clinical improvements in patients with uncontrolled, moderate-to-severe asthma enrolled from Korean centers first in the parent studies and then in TRAVERSE.

Safety findings from the current study are in line with the known dupilumab safety profile.[9,10,13] No new safety concerns were observed in any treatment groups, including those that received PBO in the parent studies and then switched to dupilumab in OLE. Although the incidence of TEAEs was numerically higher compared with the overall TRAVERSE population[13] and Japanese subgroup of patients from TRAVERSE,[17] most TEAEs were of mild-to-moderate intensity.

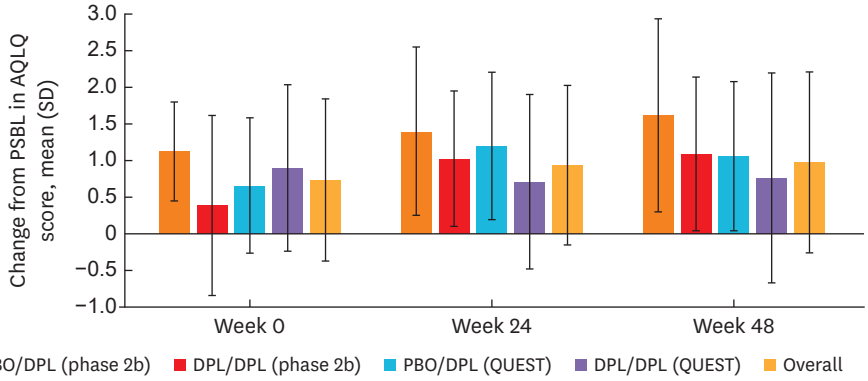
https://doi.org/10.4168/aair.2024.16.4.372



No. of patients			
PBO/DPL (phase 2b)	4	4	4
DPL/DPL (phase 2b)	17	17	17
PBO/DPL (QUEST)	19	19	17
DPL/DPL (QUEST)	31	34	30
Overall	71	74	68

ACQ-5 score at PSBL, mean (SD)	PBO/DPL (phase 2b)	DPL/DPL (phase 2b)	PBO/DPL (QUEST)	DPL/DPL (QUEST)	Overall
	2.35 (0.72)	2.24 (0.39)	2.28 (0.43)	2.30 (0.64)	2.28 (0.53)

A



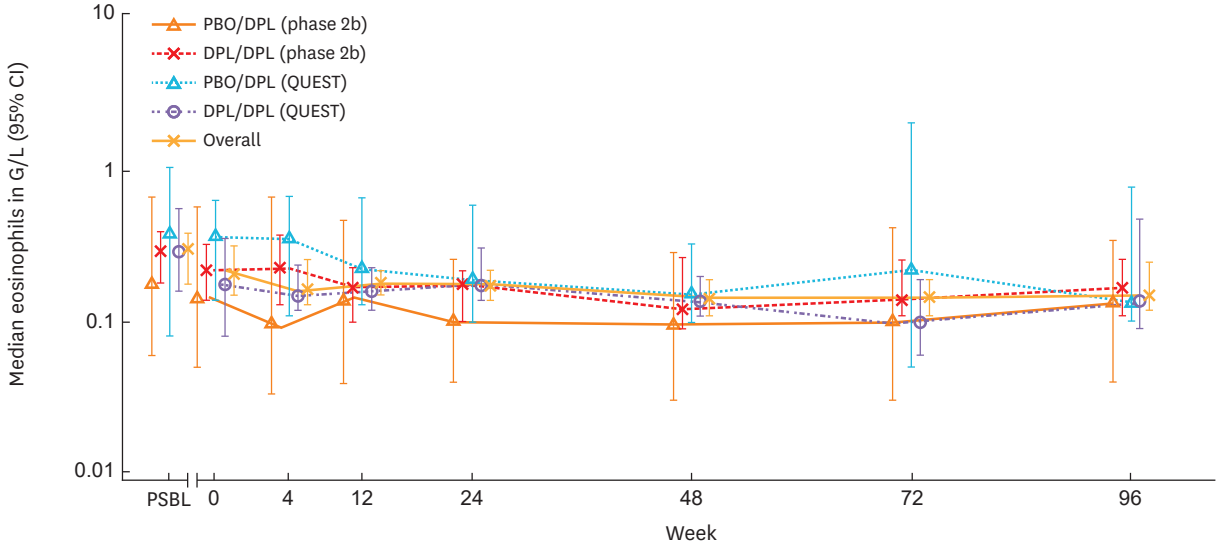
No. of patients			
PBO/DPL (phase 2b)	4	4	4
DPL/DPL (phase 2b)	16	17	17
PBO/DPL (QUEST)	17	16	15
DPL/DPL (QUEST)	33	33	29
Overall	70	70	65

ACLQ score at PSBL, mean (SD)	PBO/DPL (phase 2b)	DPL/DPL (phase 2b)	PBO/DPL (QUEST)	DPL/DPL (QUEST)	Overall
	3.99 (1.39)	3.73 (0.90)	4.62 (0.74)	4.82 (1.13)	4.46 (1.09)

B

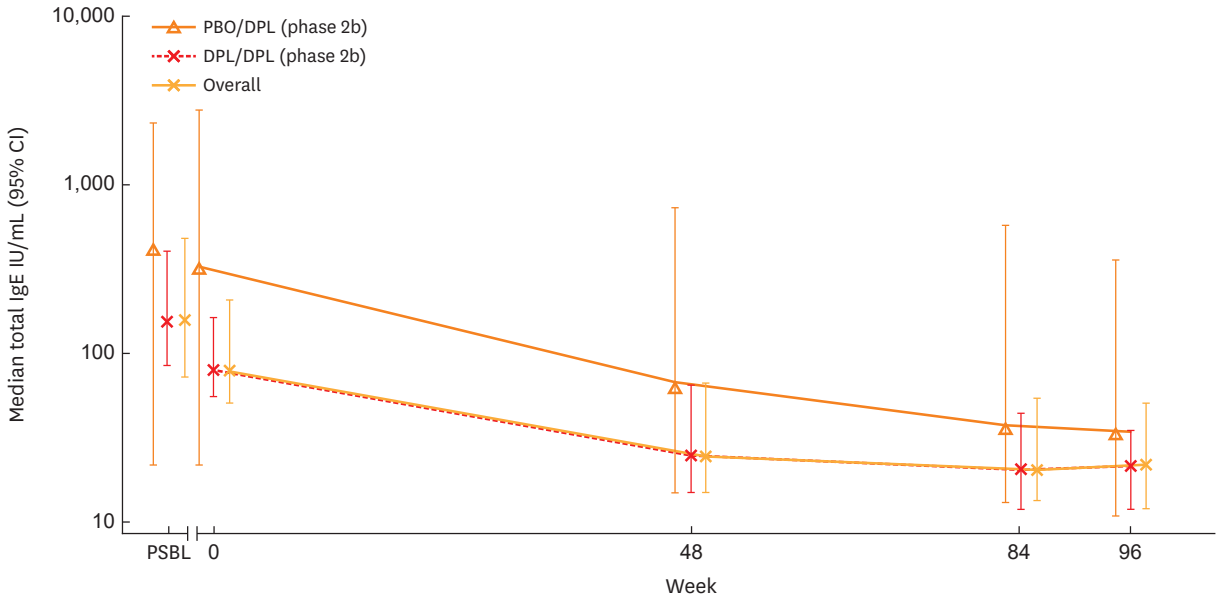
Fig. 3. Mean change from PSBL in ACQ-5 and AQLQ global scores over time in exposed patients from phase 2b and QUEST who were recruited from Korean centers and rolled over into TRAVERSE. (A) Mean change from PSBL in ACQ-5 score over time and (B) mean change from PSBL in AQLQ global score over time. For the patients from the phase 2b study, there was a gap (≥ 16 weeks) between the last dose in the phase 2b study and the first dose in TRAVERSE, because the patients needed to complete the 16-week follow-up of phase 2b study to enroll in TRAVERSE. Asthma control using the ACQ-5 (on a scale of 0–6, where high scores represent lower asthma control) and health-related quality of life using the AQLQ (on a scale of 0–7, where high scores represent less impairment). PSBL, parent study baseline; ACQ-5, 5-item Asthma Control Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; DPL, dupilumab; PBO, placebo; SD, standard deviation.

https://doi.org/10.4168/aair.2024.16.4.372



No. of patients								
PBO/DPL (phase 2b)	4	4	4	4	4	4	4	4
DPL/DPL (phase 2b)	17	16	13	17	17	17	17	17
PBO/DPL (QUEST)	19	17	18	18	18	17	6	6
DPL/DPL (QUEST)	34	31	34	32	31	30	14	14
Overall	74	68	69	71	70	68	41	41

A



No. of patients					
PBO/DPL (phase 2b)	4	4	4	4	4
DPL/DPL (phase 2b)	17	17	17	17	17
Overall	21	21	21	21	21

B

Fig. 4. Inflammatory biomarkers in exposed patients from phase 2b and QUEST who were recruited from Korean centers and rolled over into TRAVERSE. (A) Median (95% CI) blood eosinophils (G/L) over time up to Week 96 and (B) median (95% CI) total IgE (IU/mL) over time in patients from phase 2b study. For the patients from the phase 2b study, there was a gap (≥ 16 weeks) between the last dose in the phase 2b study and the first dose in TRAVERSE, because the patients needed to complete the 16-week follow-up of phase 2b study to enroll in TRAVERSE.
CI, confidence interval; DPL, dupilumab; IgE, immunoglobulin E; PBO, placebo; PSBL, parent study baseline.

https://doi.org/10.4168/aair.2024.16.4.372

Compared with the overall TRAVERSE population,[13] the incidence rate of eosinophilia was low in this analysis; no causal association was established between eosinophilic events and dupilumab. Further, there were no clinical events associated with eosinophilia.

In addition, the incidence of persistent ADA response was low in this subanalysis which is in line with what was observed in the overall TRAVERSE population[13] and the Japanese subgroup of patients from TRAVERSE[17]; none of these patients showed high titers for ADA. One patient with positive NAb status showed a slight decline in lung function compared with baseline. However, it was not confirmed whether this effect was attributable to the positive NAb status. Consistent with the overall TRAVERSE population,[13] no clinically significant effect of ADA status was observed on safety or efficacy outcomes analyzed in this study.

Dupilumab showed a significant reduction in AER and improvements in FEV1, asthma control, and quality of life in the parent studies compared with PBO,[9,10] and these benefits were sustained in the TRAVERSE OLE study.[13] Compared with the overall TRAVERSE population and the Japanese subgroup from TRAVERSE who showed AER < 0.5 during TRAVERSE,[13,17] the magnitude of reduction during the treatment period in AER was slightly lower (AER < 1 in all groups) in the current subpopulation, with an unadjusted AER of 0.470 in the overall group during the treatment period.

Improvement in FEV1 was observed as early as week 2 in TRAVERSE, in both PBO/DPL and DPL/DPL groups, with a comparable mean FEV1 between these groups; the effect was sustained throughout the 96-week treatment period. This effect was more prominent in patients from the QUEST study (63% and 42% improvement from PSBL at week 96 in PBO/DPL and DPL/DPL groups, respectively) than those from the phase 2b study (27% and 22%, in PBO/DPL and DPL/DPL groups, respectively), which could be due to the 16-week follow-up period in the 2b study (this period was 19–25 weeks for patients in this analysis), during which patients did not receive treatment, before dupilumab initiation in TRAVERSE. Compared with the overall TRAVERSE population, in which mean changes in FEV1 from PSBL at week 96 ranged from 0.22 ± 0.44 L to 0.33 ± 0.44 L,[13] FEV1 improvements were numerically higher in this subpopulation (ranging from 0.33 ± 0.34 L to 0.80 ± 0.32 L). At week 96, the FEV1 levels improved by 0.39 L (PBO/DPL) and 0.33 L (DPL/DPL) from PSBL in phase 2b patients and by 0.80 L (PBO/DPL) and 0.51 L (DPL/DPL) in QUEST patients. These results demonstrate the efficacy of dupilumab in patients who received placebo in parent studies and switched to dupilumab in TRAVERSE and maintenance of efficacy in patients who received dupilumab in parent studies and continued receiving dupilumab in TRAVERSE. FEV1 improvements seen in this subgroup analysis were comparable with those seen in the Japanese subgroup analysis of the TRAVERSE study,[17] and are in line with those seen in a previous *post hoc* analysis of Korean patients in QUEST.[19]

During the OLE, improvements in ACQ-5 and AQLQ scores were observed in all treatment groups irrespective of the treatment received in the parent study, as in the overall exposed population and Japanese subgroup of patients from TRAVERSE.[13,17] Findings from the analysis of levels of inflammatory biomarkers (eosinophils and total IgE) also confirmed sustained efficacy of dupilumab in this subpopulation in the OLE study.

Overall, the safety and efficacy outcomes from the current subgroup analysis were consistent with those observed in the overall cohort of TRAVERSE and other previous studies, including the *post hoc* analysis of the Japanese patient population in TRAVERSE and QUEST and the

https://doi.org/10.4168/aair.2024.16.4.372

post hoc analysis of Korean patients in QUEST.[17,19,20] Taken together, these results suggest that dupilumab is safe and efficacious in a broad cohort of patients, including those from Korea that belong to the Asian race and non-Hispanic ethnicity. No clinically significant impact of ethnicity on safety and efficacy parameters was seen in this study. Further, low levels of ADA and NAb reported in this analysis suggest that dupilumab may provide sustained effects in this subgroup of patients. Local registry-based research is ongoing (KoSAR Biologics registry) to assess the efficacy and safety of biologics in real-world practice in Korea.[4]

The current study has a few limitations: it was a *post hoc* analysis of an OLE study; the non-randomized and unblinded nature of the OLE study might have introduced treatment bias. The sample size was small in all groups, which limits the generalizability of the findings from this study and precludes any meaningful comparisons. Dupilumab dose and treatment duration were different in the parent studies from the OLE study. Patients entered TRAVERSE on a voluntary basis; patients in the dupilumab group in the parent study who responded to treatment may have been more likely to continue in the OLE study. Patients from the phase 2b study were off treatment for 16 weeks to 1 year before reinitiating dupilumab treatment in the OLE study. Change in total IgE levels was not assessed in patients rolled over from QUEST.

In conclusion, the results of this subgroup analysis validate the long-term efficacy and safety of dupilumab in patients enrolled from Korean centers, further strengthening the evidence for the efficacy and safety of dupilumab in patients with uncontrolled, moderate-to-severe asthma.

ACKNOWLEDGMENTS

These analyses were funded by Sanofi and Regeneron Pharmaceuticals, Inc. The authors would like to thank Christine Taniou and Carole Mercier of Axial Group for their support with statistical analyses. Manuscript writing and editorial assistance for this manuscript was provided by Sindhu Doppalapudi, PhD, of Sanofi, according to the Good Publication Practice guideline.

SUPPLEMENTARY MATERIALS

Supplementary Table S1

Summary of treatment-emergent SAEs and TEAEs leading to permanent treatment discontinuation by primary system organ class and preferred term—exposed patients from phase 2b and QUEST who were recruited from Korean centers and rolled over into TRAVERSE

Supplementary Table S2

Summary of ADA incidence—exposed patients from phase 2b and QUEST who were recruited from Korean centers and rolled over into TRAVERSE

Supplementary Table S3

Summary of NAb status—exposed patients from phase 2b and QUEST who were recruited from Korean centers and rolled over into TRAVERSE

Supplementary Table S4

Findings from responder analysis—exposed patients from phase 2b and QUEST who were recruited from Korean centers and rolled over into TRAVERSE

https://doi.org/10.4168/aair.2024.16.4.372

REFERENCES

1. Porsbjerg C, Melén E, Lehtimäki L, Shaw D. Asthma. Lancet 2023;401:858-73. PUBMED | CROSSREF
2. Moore WC, Peters SP. Severe asthma: an overview. J Allergy Clin Immunol 2006;117:487-94. PUBMED | CROSSREF
3. Global Initiative for Asthma (GINA). Diagnosis and management of difficult-to-treat and severe asthma in adolescent and adult patients [Internet]. Fontana (WI): GINA; 2019 [cited 2023 Sep 15]. Available from: https://ginasthma.org/wp-content/uploads/2019/04/GINA-Severe-asthma-Pocket-Guide-v2.0-wms-1.pdf.
4. Kim SH, Lee H, Park SY, Park SY, Song WJ, Kim JH, et al. The Korean Severe Asthma Registry (KoSAR): real world research in severe asthma. Korean J Intern Med 2022;37:249-60. PUBMED | CROSSREF
5. Lee E, Kim A, Ye YM, Choi SE, Park HS. Increasing prevalence and mortality of asthma with age in Korea, 2002-2015: a nationwide, population-based study. Allergy Asthma Immunol Res 2020;12:467-84. PUBMED | CROSSREF
6. Fahy JV. Type 2 inflammation in asthma--present in most, absent in many. Nat Rev Immunol 2015;15:57-65. PUBMED | CROSSREF
7. Hamilton JD, Harel S, Swanson BN, Brian W, Chen Z, Rice MS, et al. Dupilumab suppresses type 2 inflammatory biomarkers across multiple atopic, allergic diseases. Clin Exp Allergy 2021;51:915-31. PUBMED | CROSSREF
8. Jin HJ. Biological treatments for severe asthma. Yeungnam Univ J Med 2020;37:262-8. PUBMED | CROSSREF
9. Castro M, Corren J, Pavord ID, Maspero J, Wenzel S, Rabe KF, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. N Engl J Med 2018;378:2486-96. PUBMED | CROSSREF
10. Wenzel S, Castro M, Corren J, Maspero J, Wang L, Zhang B, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting β2 agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. Lancet 2016;388:31-44. PUBMED | CROSSREF
11. Sanofi. Evaluation of dupilumab in patients with severe steroid dependent asthma (VENTURE) [Internet]. Bethesda (MD): National Library of Medicine; 2019 [cited 2023 Sep 15]. Available from: https://clinicaltrials.gov/ct2/show/NCT02528214.
12. Sanofi. Long-term safety evaluation of dupilumab in patients with asthma (LIBERTY ASTHMA TRAVERSE) [Internet]. Bethesda (MD): National Library of Medicine; 2022 [cited 2023 Sep 15]. Available from: https://clinicaltrials.gov/ct2/show/NCT02134028.
13. Wechsler ME, Ford LB, Maspero JF, Pavord ID, Papi A, Bourdin A, et al. Long-term safety and efficacy of dupilumab in patients with moderate-to-severe asthma (TRAVERSE): an open-label extension study. Lancet Respir Med 2022;10:11-25. PUBMED | CROSSREF
14. Sanofi. Evaluation of dupilumab's effects on airway inflammation in patients with asthma (EXPEDITION) [Internet]. Bethesda (MD): National Library of Medicine; 2022 [cited 2023 Sep 15]. Available from: https://clinicaltrials.gov/ct2/show/NCT02573233.
15. Sanofi. An evaluation of dupilumab in patients with moderate to severe uncontrolled asthma [Internet]. Bethesda (MD): National Library of Medicine; 2017 [cited 2023 Sep 15]. Available from: https://clinicaltrials.gov/ct2/show/NCT01854047.
16. Sanofi. Evaluation of dupilumab in patients with persistent asthma (Liberty Asthma Quest) [Internet]. Bethesda (MD): National Library of Medicine; 2018 [cited 2023 Sep 15]. Available from: https://clinicaltrials.gov/ct2/show/NCT02414854.
17. Tohda Y, Nakamura Y, Fujisawa T, Ebisawa M, Msihid J, Djandji M, et al. Efficacy of dupilumab in patients with uncontrolled, moderate-to-severe asthma recruited from Japanese centers in the phase 3 LIBERTY ASTHMA TRAVERSE study. Allergol Int 2023;72:89-99. PUBMED | CROSSREF
18. Juniper EF, Svensson K, Mörk AC, Ståhl E. Measurement properties and interpretation of three shortened versions of the asthma control questionnaire. Respir Med 2005;99:553-8. PUBMED | CROSSREF
19. Rhee CK, Park JW, Park HW, Cho YS. Effect of dupilumab in Korean patients with uncontrolled moderate-to-severe asthma: a LIBERTY ASTHMA QUEST sub-analysis. Allergy Asthma Immunol Res 2022;14:182-95. PUBMED | CROSSREF
20. Tohda Y, Nakamura Y, Fujisawa T, Ebisawa M, Arima K, Miyata M, et al. Dupilumab efficacy and safety in Japanese patients with uncontrolled, moderate-to-severe asthma in the phase 3 LIBERTY ASTHMA QUEST study. Allergol Int 2020;69:578-87. PUBMED | CROSSREF