Supplementary Material

The impact of lebrikizumab on vaccine-induced immune responses: results from a phase 3 study in adult patients with moderate-to-severe atopic dermatitis

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Table S1: Significant Protocol Deviations Leading to Participant Exclusion From Per-Protocol Set

Significant Protocol Deviation	PBO N = 127 n (%)	LEB 250mg Q2W N = 127 n (%)	Total N = 254 n (%)
Used prohibited treatment that required permanent discontinuation of the study drug	4 (3.1)	3 (2.4)	7 (2.8)
Missed both Week 0 and Week 12 or Week 16 vaccine titers results	38 (29.9)	13 (10.2)	51 (20.1)
Missing Tdap vaccine response data	41 (32.3)	14 (11.0)	55 (21.7)
Missing meningococcal vaccine response data	39 (30.7)	21 (16.5)	60 (23.6)
Have not been compliant with the dosing regimen (i.e., participants must receive 80% of the expected injections of study drug and both of the vaccines during participation in the study)	31 (24.4)	9 (7.1)	40 (15.7)
Exceeded the out-of-the-visit window at the Week 16 visit (Visit 10) by more than 7 days	3 (2.4)	2 (1.6)	5 (2.0)
Other SPDs[a]	7 (5.5)	3 (2.4)	10 (3.9)
Excluded patients due to GCP issues in 2 sites	5 (3.9)	2 (1.6)	7 (2.8)
Per-Protocol Set[b]	81 (63.8)	107 (84.3)	188 (74.0)

[a] Other significant protocol deviations (SPDs) are events that could have possibly impacted on precise evaluation of the primary objective. The primary objective of study J2T-MC-KGAK was to compare the sero-responses to the Tdap and MCV between lebrikizumab-treated and placebo-treated participants with moderate-to-severe atopic dermatitis.

[b] Per-protocol set is all safety population participants without any significant protocol deviations, where safety population includes all randomized participants who received at least one dose of study treatment.

Table S2. Concomitant treatments

	Placebo Q2W (N=122)	Lebrikizumab 250 mg Q2W (N=125)
Concomitant Treatments		
Topical corticosteroids	18 (14.8)	11 (8.8)
Low-Moderate Potency TCS[1]	17 (13.9)	9 (7.2)
Alclometasone	1 (0.8)	0
Hydrocortisone	4 (3.3)	4 (3.2)
Triamcinolone	15 (12.3)	6 (4.8)
High Potency TCS	2 (1.6)	2 (1.6)
Clobetasol	1 (0.8)	0
Desoximetasone	1 (0.8)	0
Fluocinonide	0	1 (0.8)
Ulovetasol	0	1 (0.8)

[1]Low-Moderate Potency TCS use was not considered rescue therapy in this trial.

Table S3. Description and Derivation of Efficacy/Health Outcomes Measures and Endpoints

Measure	Description	Variable	Imputation Approach if Missing Components
Anti-tetanus toxoid IgG antibody concentration	Anti-tetanus toxoid IgG antibody concentration is a laboratory test result.	Anti-tetanus IgG antibody concentration	Single item, missing if missing.
		Booster response to tetanus toxoid 4 weeks after the administration of the Tdap vaccine (Week 16)	Single item, missing if missing.
MCV (Group C serum bactericidal antibodies)	MCV (Group C serum bactericidal antibodies) is a laboratory test result.	MCV (Group C serum bactericidal antibodies)	Single item, missing if missing.
		Positive antibody response to MCV (Group C serum bactericidal antibodies) 4 weeks after the administration of the vaccine (Week 16)	Single item, missing if missing.
Investigator's Global Assessment (IGA)	The IGA is a static assessment and rates the severity of the participant's AD. The IGA is comprised of a 5-point scale ranging from 0 (clear) to 4 (severe), and a score is selected using descriptors that best describe the overall appearance of the lesions at a given time point.	IGA score	Single item, missing if missing.
		IGA (0,1) with ≥2-point improvement IGA (0)	Missing if baseline or observed value is missing. Single item, missing if missing.
	The EASI scoring system uses a defined process (Steps 1 through 5 below) to grade the severity of the signs	EASI score	N/A – partial assessments cannot be saved.

Measure	Description	Variable	Imputation Approach if Missing Components
Eczema Area and Severity Index (EASI)	of eczema and the extent affected. The extent of disease (percentage of skin affected: 0 = 0%; 1 = 1% to 9%; 2 = 10% to 29%; 3 = 30% to 49%; 4 = 50% to 69%; 5 = 70% to 89%; 6 = 90% to 100%) and the severity of 4 clinical signs (erythema, edema/papulation, excoriation, and lichenification), each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head and neck, trunk, upper limbs, and lower limbs). Half scores are allowed between Severities 1, 2 and 3. Each body site will have a score that ranges from 0 to 72, and the final EASI score will be obtained by weight-averaging these 4 scores. Hence, the final EASI score will range from 0 to 72 for each time point.	Change from baseline in EASI score Percent change from baseline EASI score	Missing if baseline or observed value is missing.
		EASI 50	Missing if baseline or observed value is missing.
		EASI 75	Missing if baseline or observed value is missing.
		EASI 90	Missing if baseline or observed value is missing.
Body Surface Area (BSA)	The BSA assessment estimates the extent of disease or skin involvement with respect to AD and is expressed as a percentage of total body surface. BSA will be determined by the Investigator or designee using the participant palm = 1% rule.	BSA score	N/A – partial assessments cannot be saved.
		Change from baseline in BSA score	Missing if baseline or observed value is missing.
Pruritus Numeric Rating Scale (NRS)	The Pruritus NRS is a an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating “No itch” and 10 indicating “Worst itch imaginable.” Assessments will be recorded daily by the participant using an electronic diary.	Pruritus NRS prorated weekly mean score	Weekly mean score missing if the participant has no Pruritus NRS responses within the week.
		Change from baseline in Pruritus NRS prorated weekly mean score Percent change from baseline in Pruritus NRS prorated weekly mean score	Missing if baseline or observed value is missing.
		4-point improvement in Pruritus NRS prorated	Missing if baseline is missing or observed value is missing.

Measure	Description	Variable	Imputation Approach if Missing Components
		weekly mean score	
Sleep-loss due to pruritus	Sleep-loss due to pruritus will be assessed by the participant. Participants rate their sleep based on a 5-point Likert scale (0 [not at all] to 4 [unable to sleep at all]). Assessments will be recorded daily by the participant using an electronic diary.	Sleep-loss prorated weekly mean score	Weekly mean score missing if the participant has no Sleep-loss due to pruritus responses within the week.
		Change from baseline in Sleep-loss prorated weekly mean score Percent change from baseline in Sleep-loss prorated weekly mean score	Missing if baseline or observed value is missing.
		2-point improvement in Sleep-loss prorated weekly mean score	Missing if baseline is missing or observed value is missing.
Skin Pain NRS	Skin Pain NRS is a participant-administered, validated, 11-point horizontal scale anchored at 0 and 10, with 0 representing “no pain” and 10 representing “worst pain imaginable.” Overall severity of a participant’s skin pain is indicated by selecting the number that best describes the worst level of skin pain in the past 24 hours. Assessments will be recorded daily by the participant using an electronic diary.	Skin Pain NRS prorated weekly mean score	Weekly mean score missing if the participant has no Skin Pain NRS responses within the week.
		Change from baseline in Skin Pain NRS prorated weekly mean score Percent change from baseline in Skin Pain NRS prorated weekly mean score	Missing if baseline or observed value is missing.
		4-point improvement in Skin Pain NRS prorated weekly mean score	Missing if baseline is missing or observed value is missing.

Measure	Description	Variable	Imputation Approach if Missing Components
Patient-Oriented Eczema Measure (POEM)	The POEM is a 7-item, validated, questionnaire used by the participant to assess disease symptoms over the last week. The participant is asked to respond to 7 questions on skin dryness, itching, flaking, cracking, sleep-loss, bleeding, and weeping. All 7 answers carry equal weight with a total possible score from 0 to 28 (answers scored as: No days = 0; 1 to 2 days = 1; 3 to 4 days = 2; 5 to 6 days = 3; everyday = 4). A high score is indicative of a poor quality of life. POEM responses will be captured using an electronic diary and transferred into the clinical database.	POEM score	If a single question is left unanswered, then that question is scored as 0. If more than 1 question is unanswered, then the tool is not scored. If more than 1 response is selected, then the response with the highest score is used.
		Change from baseline in POEM score	Missing if baseline or observed value is missing.
		4-point improvement	Missing if baseline is missing or observed value is missing.
Patient-Reported Outcomes Measurement Information System (PROMIS)	PROMIS is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. Pediatric and tools for anxiety and depression.	PROMIS anxiety total score PROMIS depression total score	Total score can be derived even with partial response as instrument use item response theory method.
		Change from baseline in PROMIS anxiety total score Change from baseline in PROMIS depression total score	Missing if baseline or observed value is missing.