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Eric L. Simpson, MD, Jane R. Parnes, MD, Dewei She, PhD, Sarah Crouch, BA (Hons), William Rees, PhD, May Mo, MS, René van der Merwe, MBChB



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ORIGINAL ARTICLE**Tezepelumab, an anti-TSLP monoclonal antibody, in the treatment of moderate to severe atopic dermatitis: A randomized phase 2a clinical trial**

Eric L. Simpson, MD,^a Jane R. Parnes, MD,^b Dewei She, PhD,^{c*} Sarah Crouch, BA (Hons),^d William Rees, PhD,^{c*} May Mo, MS,^b René van der Merwe, MBChB^d

^a*Oregon Health and Science University, Portland, OR, USA;* ^b*Amgen Inc, Thousand Oaks, CA, USA;* ^c*MedImmune, Gaithersburg, MD, USA;* ^d*MedImmune, Cambridge, UK*

**Employee of MedImmune at the time the study was conducted. Current affiliation: Viela Bio, Gaithersburg, MD, USA*

Corresponding author: Dr. Eric Simpson, MD, Oregon and Science University, Portland, Oregon.

Tel: +1 503 494 2121; **Fax:** +1 503 494 6907; **E-mail:** simpsons@ohsu.edu

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ABSTRACT

Background: Tezepelumab (AMG 157/MEDI9929), a first-in-class monoclonal antibody, targets thymic stromal lymphopoietin, a cytokine implicated in atopic dermatitis (AD) pathogenesis.

Objective: Evaluate efficacy and safety of tezepelumab in adults with moderate to severe AD.

Methods: In this phase 2a study (NCT02525094), 113 patients were randomized 1:1 to subcutaneous tezepelumab 280 mg or placebo every 2 weeks, plus Class 3 topical corticosteroids (TCS). The primary endpoint was the Week-12 response rate for a $\geq 50\%$ reduction in Eczema Area and Severity Index (EASI50). Secondary endpoints including EASI75, Investigator's Global Assessment, Scoring of Atopic Dermatitis (SCORAD) 50, SCORAD75, pruritus numeric rating and 5-D itch scales, and exploratory endpoints (including EASI90) were assessed at Week 12, and Week 16 (*post hoc*).

Results: A numerically greater percentage of tezepelumab plus TCS-treated patients achieved EASI50 (64.7%) versus placebo plus TCS (48.2%; $P = .091$). Numerical improvements over placebo were demonstrated for Week 12 secondary and exploratory endpoints, with further improvements at Week 16. Treatment-emergent adverse events were similar between treatment groups.

Limitations: Greater than expected response rates in placebo-treated patients were possibly attributable to TCS.

Conclusion: Although not statistically significant, numerical improvements over placebo for all Week 12 endpoints were demonstrated, with greater Week 16 responses.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, complex inflammatory skin condition characterized by pruritic eczematous skin lesions, impacting patients' and their families' quality of life.¹⁻³ Patients with mild AD can usually control their condition by avoiding disease triggers and applying emollients and topical corticosteroids (TCS).⁴ AD onset is often accompanied by other allergic disease manifestations⁵ and, as recently identified, is associated with increased risk of cardiovascular disease versus patients without AD,⁶ suggesting the condition is a complex systemic disorder. Patients with moderate to severe AD may benefit from systemic therapy^{4,7,8}; however, more robust studies are required to evaluate their efficacy and long-term safety.⁹

Thymic stromal lymphopoietin (TSLP), an epithelial-cell-derived cytokine, is produced in response to pro-inflammatory stimuli. TSLP-activated dendritic cells induce production of T helper (Th) 2 cytokines interleukin (IL)-4, IL-5, IL-13 and tumor necrosis factor- α .¹⁰ Increasing evidence supports a role for Th2 inflammation in AD pathogenesis¹¹⁻¹⁷; recent studies of dupilumab (an IL-13/IL-4 inhibitor) demonstrated substantial responses in patients with AD. TSLP could be a key target to control AD-associated inflammation and skin barrier disruption, the pathogenesis of which is associated with these downstream Th2 cytokines and immunomodulating proteins. Serum periostin and dipeptidyl peptidase-4 (DPP-4) are considered biomarkers of IL-13 axis activation^{18,19} and may predict response to molecules targeting TSLP, which is upstream of IL-13.¹⁰ Similarly, immunoglobulin E (IgE) and chemokine (C-C motif) ligand 17/thymus- and activation-regulated chemokine (CCL17/TARC) are upregulated by TSLP^{10,20} and could reflect increased TSLP activity.

Tezepelumab (AMG 157/MEDI9929) is a first-in-class, fully human immunoglobulin G2 λ monoclonal antibody that specifically binds TSLP and prevents interaction with its receptor complex. In the phase 2b PATHWAY study, tezepelumab demonstrated significant reductions in annual asthma exacerbation rate versus placebo in patients with uncontrolled asthma, irrespective of baseline biomarker status.

104 Here, we evaluate the efficacy and safety of tezepelumab in patients with moderate to
105 severe AD treated with continuous concomitant Class 3²¹ TCS. The effects of tezepelumab
106 in patient-reported outcomes and impact of serum biomarkers on treatment response are
107 also reported.

108

METHODS

Study Design

This phase 2a, randomized, double-blind, placebo-controlled study (ALLEVIAD; NCT02525094) was conducted at 26 centers in Australia, Canada, Germany, Hungary, New Zealand, and the USA, in accordance with the Declaration of Helsinki, International Conference on Harmonization guidelines, and relevant laws and regulations. The protocol and amendments were approved by appropriate institutional review boards and independent ethics committees. Written informed consent was obtained from all patients.

Eligible patients received maintenance Class 3 (high-strength) TCS at least once daily on lesional skin during the 2-week run-in period and throughout the 24-week study. Patients were stratified at randomization by their screening serum IgE concentration (<150 or ≥ 150 kU/L). Within each stratum, patients were randomized 1:1 (via central interactive voice/web response) to receive placebo or tezepelumab 280 mg subcutaneously (SC) every 2 weeks (Q2W) for 12 weeks; the last dose was at Week 10. Patients completed a 10-week safety follow-up period. Randomization, treatment administration, blinding methodology, and study termination guidelines are provided in the supplement.

Patients

Eligible patients were aged 18–75 years with a diagnosis of AD (according to Hanifin and Rajka), an Eczema Area and Severity Index (EASI) score ≥ 12 and Investigator's Global Assessment (IGA) score ≥ 3 (screening and baseline), a Scoring of Atopic Dermatitis (SCORAD) ≥ 20 , and total AD body surface area $\geq 10\%$ assessed by EASI (screening). Patients with dermatologic conditions, which might confound AD diagnosis or treatment assessment, were excluded. Detailed inclusion and exclusion criteria are provided in the supplement.

Study Endpoints

The primary efficacy endpoint was the percentage of patients achieving a $\geq 50\%$ reduction in EASI score (EASI50) from baseline to Week 12. Secondary endpoints (including patient-reported outcomes) and exploratory endpoints were measured at Week 12; full details are provided in the supplement. A *post-hoc* analysis of all endpoints was conducted at Week 16.

Safety endpoints, measured through Week 22, included treatment-emergent adverse events (TEAEs) and serious TEAEs (TESAEs). In an exploratory analysis, selected endpoints were evaluated in subgroups, defined by inflammatory markers of pathways downstream of TSLP: serum periostin, DPP-4, and CCL17/TARC, and IgE. The clinical assessments performed and methods for serum biomarker determination are detailed in the supplement.

Statistical Methods

Based on a previous study, it was estimated that a sample size of 25 patients per treatment group would provide 80% power (two-sided significance of .05) to detect a treatment difference of 40% for the primary endpoint, assuming a placebo response rate of 45%. The biomarker subpopulation was assumed to be 50% of the total population and sample size was adjusted by doubling the required number to 50 patients per treatment group.

Efficacy endpoints were analyzed in the intention-to-treat (ITT) population, defined as all patients who were randomized to, and received treatment; data were grouped by randomized treatment. Safety data were reported in the as-treated population, defined as all patients who received treatment, with data grouped by first treatment received.

Baseline demographics and safety data were summarized descriptively. Binary endpoints were analyzed at each visit using logistic regression with total serum IgE concentration and

161 baseline value as covariates. The last non-missing post-baseline value was carried forward
162 when data were missing. For patients who received prohibited or discouraged AD treatment,
163 the last response value from the day of, or prior to receipt of the therapy was carried forward.
164 Continuous endpoints were analyzed using a mixed-effect model repeated-measure
165 analysis. No multiplicity adjustments were made for secondary or exploratory analyses.
166 Exploratory analyses of biomarker data were not powered, but were pre-specified, and used
167 similar statistical methods for the primary analysis.

RESULTS

Patients

The first patient was screened on August 15, 2015 and the first patient dosed on August 29, 2015. The last patient was evaluated on July 15, 2016. Of 155 patients screened, 113 were randomized and 111 received treatment (placebo plus TCS: N = 56; tezepelumab plus TCS: N = 55) (Fig 1). Baseline demographics and clinical characteristics were similar between treatment groups (Table 1). In both groups, 84.7% of patients had childhood AD, 43.2% had childhood asthma and 39.6% had adult asthma. At the end of the treatment period, tezepelumab-treated patients had applied less TCS versus placebo (mean [standard deviation]: 323.4 [347.7] mg versus 429.3 [570.4] mg).

Efficacy Outcomes

At Week 12, a numerically greater percentage of tezepelumab plus TCS-treated patients achieved an EASI50 response (64.7%) compared with placebo plus TCS (48.2%); however, the treatment difference was not statistically significant (odds ratio [OR] (95% confidence interval [CI]), 1.97 (.90–4.33); $P = .091$; Fig 2A). Comparable improvements were seen *post hoc* at Week 16 (60.9% versus 51.9%; OR [95% CI] 1.45 [.66–3.16]; $P = .353$; Fig 2A). Similarly, a numerically greater percentage of tezepelumab plus TCS-treated patients achieved an EASI75 response at Week 12 (24.4% versus 19.8%; OR [95% CI] 1.31 [.51–3.31]; $P = .574$), with greater improvements seen at Week 16: 36.9% versus 21.9%; OR [95% CI] 2.09 [.88–5.00]; $P = .096$ (Fig 2A). In exploratory analyses, tezepelumab plus TCS-treated patients had numerical improvements over placebo in EASI90 response rates at Week 12 (11.8% versus 5.6%; OR [95% CI] 2.27 [.45–14.70]; $P = .283$) and Week 16 (20.8% versus 10.6%; OR [95% CI] 2.20 [.74–6.60]; $P = .158$; Fig 2A). A *post-hoc* analysis of change in lichenification (measured through EASI and SCORAD scoring) found no significant difference between treatment groups at any time point (Table S1).

Improvements in adjusted mean percentage improvement from baseline in EASI (total score) relative to placebo plus TCS were observed from Week 4 and maintained until Week 16 in tezepelumab plus TCS-treated patients (Fig 2B). The adjusted mean percentage difference for the improvement from baseline in EASI (95% CI) at Week 12 was 6.28 (–7.92–20.49), $P = .382$.

A numeric difference between treatment groups in IGA response rate was observed at Week 12 (19.3% versus 12.8%; OR [95% CI] 1.64 [.57–4.71]; $P = .361$). By Week 16, the improvement in IGA response rate in tezepelumab plus TCS-treated patients versus placebo plus TCS had reached a nominal P -value of $<.05$ (29.4% versus 12.9%; OR [95% CI] 2.81 [1.04–7.63]; $P = .042$ (Fig 2C).

Numeric improvements in SCORAD versus placebo were observed throughout the analysis period (Fig 2D); the adjusted mean percentage difference (95% CI) between treatment groups for improvement from baseline at Week 12 was 8.46 (–2.95–19.87); $P = .144$. Furthermore, numeric improvements versus placebo were observed in SCORAD50 or SCORAD75 response rates at Week 12: 41.0% versus 29.4%; OR (95% CI) 1.67 (.74–3.80); $P = .219$ for SCORAD50 and 9.8% versus 7.4%; OR (95% CI) 1.36 (.27–7.26); $P = .762$ for SCORAD75. Similarly, at Week 16, there was no substantial difference between treatment groups (data not shown).

Patient-Reported Outcomes

Patients receiving tezepelumab plus TCS demonstrated nominally significant improvements from baseline to Week 12 in pruritus NRS versus placebo plus TCS; adjusted mean percentage improvement (standard error [SE]): 35.53 (5.89) versus 21.05 (5.91); $P = .050$ (Fig 3). Peak pruritus NRS scores were numerically lower for tezepelumab plus TCS-treated patients at Week 12, but did not reach nominal significance: adjusted mean percentage improvement (SE): 33.54 (6.02) versus 25.41 (6.06); $P = .258$. Little improvement in pruritus

5-D itch scale score was observed in tezepelumab plus TCS-treated patients versus placebo plus TCS at Week 12 (–3.79 versus –3.85; adjusted mean difference (95% CI) .07 (–1.55–1.69) $P = .934$), or other time points analyzed (data not shown).

Safety Assessments

The safety analysis was performed on the as-treated population ($N = 111$). One patient randomized to placebo received an incorrect first dose of tezepelumab and was included in the tezepelumab group; all subsequent doses were placebo.

The incidence of TEAEs was similar between treatment groups (Table 2). Most were mild or moderate in severity (grade 1/2), while 5 (8.9%) tezepelumab plus TCS-treated and 7 (12.7%) placebo plus TCS-treated patients experienced a serious or severe TEAE ($\geq$ grade 3). No deaths were reported. The most frequent TEAE considered possibly treatment related by investigator was injection-site erythema, reported in 3 (5.4%) tezepelumab- and no placebo plus TCS-treated patients. One placebo plus TCS-treated patient experienced a treatment-related TESAE of cellulitis.

Six patients discontinued treatment due to TEAEs; all events were unrelated to study treatment. Placebo plus TCS-treated patients experienced AD worsening ($n = 3$) and eczema flare ($n = 1$) while tezepelumab plus TCS-treated patients reported AD worsening ($n = 1$) and syncope vasovagal ($n = 1$).

Exploratory Biomarker Subgroup Analyses

Tezepelumab plus TCS-treated patients who were DPP-4–high, periostin–low, CCL17/TARC–low, or IgE–high had numerically greater Week 12 responses compared with opposing biomarker subgroups. The percentage (adjusted) of tezepelumab plus TCS– versus placebo plus TCS-treated patients with an EASI50 response was 72.4% versus 56.5%; OR [95% CI] 2.03 [.63–6.51] (DPP-4–high patients), 76.0% versus 46.4%; OR [95% CI] 3.62 [1.11–11.88] (periostin–low patients), 79.2% versus 50.0%; OR [95% CI] 3.98

247 [1.14–13.95] (CCL17/TARC–low patients) and 65.9% versus 46.0%; OR [95% CI] 2.28
248 [0.98–5.33] (IgE–high patients). Similar results were demonstrated for EASI75, EASI90 and
249 IGA analyses (data not shown).

DISCUSSION

Tezepelumab 280 mg SC Q2W plus TCS did not demonstrate statistically significant improvements in patients with moderate to severe AD versus placebo plus TCS, as assessed by EASI50 at Week 12. A trend towards improvement for tezepelumab plus TCS-treated patients versus placebo plus TCS was observed for almost all endpoints. At Week 16, a trend towards a superior EASI75 response, and stronger improvement in IGA response in tezepelumab plus TCS-treated patients versus placebo plus TCS was observed.

The limited efficacy demonstrated on inflammatory signs and itch via TSLP blockade is surprising as preclinical studies implicate a role for TSLP in AD. In AD mouse models, TSLP directly stimulates Th2 cytokine production leading to inflammation,²² and collagen production leading to skin fibrosis.²³ Genetic studies have identified associations between *TSLP* polymorphisms and patient susceptibility to AD development, and TSLP protein is overexpressed in the keratinocytes of patients with chronic or acute AD.¹⁰ There is also evidence that TSLP causes pruritus in mice via neurostimulatory effects.^{24,25} In this study, little improvement in pruritus was seen in tezepelumab plus TCS-treated patients. Conversely, dupilumab improved pruritus in a phase 3 study of patients with moderate to severe AD,¹⁴ indicating that IL-4 may play a more fundamental role than TSLP in blocking signals within itch neurons. However, it should be noted that TSLP is upstream of IL-4¹⁰ and therefore should diminish this cytokine, thereby affecting pruritus. It is possible that this inhibition may not be as complete as for IL-4 receptor alpha blockade by dupilumab. The effect of tezepelumab on pruritus here could have been masked by concomitant high-strength TCS use.

Limitations of the study that may have confounded results included the patient population selected, TCS use and length of treatment. Patients were not required to be refractory to TCS at baseline, and received TCS during the run-in and treatment periods. This may have contributed to the placebo effect seen. A recent AD study revealed continued TCS use yields

substantial responses in placebo-treated patients.²⁶ In our study, placebo-treated patients applied greater TCS amounts during treatment versus tezepelumab-treated patients. All patients applied high-strength TCS during the 2-week run-in period, further blunting any differential effect due to study treatment. It is possible that a tezepelumab monotherapy study might uncover a more definitive efficacy signal. Alternatively, an adjunctive TCS study designed to exclude TCS responders by utilizing a longer run-in period and/or lower potency TCS might demonstrate improved results. Furthermore, only a small number of enrolled patients had severe disease (20%), while most had moderate AD (determined by IGA score). Given the upstream mechanism of action of TSLP, a longer treatment period may reveal greater improvements in AD symptoms beyond Week 12. Finally, the dose used in the study (tezepelumab 280 mg) was selected following the phase 1 study (NCT00757042) and from our results, we are unsure if complete inhibition of TSLP was demonstrated.

AD is a heterogeneous disease, and understanding this may allow for identification of patient subgroups that respond better to immune-modifying therapies. We found DPP-4–high, periostin–low or IgE–high patients demonstrated greater treatment differences in clinical response at Weeks 12 and 16 versus opposing biomarkers. Similar results were seen in the CCL17/TARC–low subgroup; given the role of IL-13 in enhancing CCL17/TARC expression²⁷, these findings are somewhat unexpected and possibly attributed to confounding concomitant TCS treatment. CCL17/TARC concentration has been reported to decrease following TCS therapy. Therefore, the run-in period where patients received TCS may have led to reported baseline CCL17/TARC concentrations being lower than unreported screening values, identifying a potential responder population. Analyses of biomarker subgroups in this study were not powered, but were pre-specified.

The incidence of TEAEs was similar between treatment groups, and the safety profile reported was comparable to that described in the phase 2b PATHWAY trial in patients with uncontrolled asthma.

In conclusion, patients with moderate to severe AD achieved numerical improvements over placebo in Week-12 EASI50 responses when treated with the anti-TSLP monoclonal antibody tezepelumab plus TCS; however, these improvements were not statistically significant. Numerical improvements were seen across several clinical and patient-reported endpoints, and greater efficacy in biomarker-defined subgroups suggest potential benefits in TSLP blockade. Given the preclinical evidence establishing the role of TSLP in AD, additional clinical studies are required to validate these findings.

Author contributions

Dr Simpson contributed to study design, data gathering, generation and analysis, manuscript preparation and review, and approved the final version of the manuscript for publication. Dr Parnes contributed to study design, data gathering and analysis, manuscript preparation and review, and approved the final version of the manuscript for publication. Dr She contributed to data gathering, generation and analysis, manuscript preparation and review, and approved the final version of the manuscript for publication. Ms Crouch contributed to study design, data gathering, manuscript preparation and review, and approved the final version of the manuscript for publication. Dr Rees contributed to data gathering, generation and analysis, manuscript preparation and review, and approved the final version of the manuscript for publication. Ms Mo contributed to data analysis, manuscript preparation and review, and approved the final version of the manuscript for publication. Dr van der Merwe contributed to data analysis, manuscript preparation and review, and approved the final version of the manuscript for publication.

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Abbreviations

AD, atopic dermatitis; CCL17/TARC, ligand 17/thymus- and activation-regulated chemokine;
CI, confidence interval; DPP-4, dipeptidyl peptidase-4; EASI, Eczema Area and Severity
Index; IGA, Investigator's Global Assessment; IgE, immunoglobulin E; IL, interleukin; ITT,
intention-to-treat; NRS, numeric rating scale; OR, odds ratio; Q2W, every 2 weeks; SC,
subcutaneously; SCORAD, Scoring of Atopic Dermatitis; SE, standard error; TCS, topical
corticosteroids; TEAEs, treatment-emergent adverse events; TESAEs, serious TEAEs; Th, T
helper; TSLP, thymic stromal lymphopoietin.

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Figures

Figure 1. Patient disposition.

TCS, topical corticosteroid.

Figure 2. Percentage of patients who achieved an EASI50, EASI75 and EASI90 response at Week 12 and 16 (A); percentage improvement from baseline in EASI (total score) over time (B); percentage of patients with an IGA response at Week 12 and 16 (C); percentage improvement from baseline in SCORAD (total score) over time (D) for the ITT population.

*Nominal $p < 0.05$ for the comparison with placebo.

Patients were considered to be IGA responders if they had an IGA response of 0 or 1 and a reduction of two grades or more from baseline to Week 12. IGA severity categories are 0 (clear), 1 (almost clear), 2 (mild), 3 (moderate), 4 (severe), and 5 (very severe).

EASI50, $\geq 50\%$ reduction in Eczema Area and Severity Index score; EASI75, $\geq 75\%$ reduction in Eczema Area and Severity Index score; EASI90, $\geq 90\%$ reduction in Eczema Area and Severity Index score; IGA, Investigator's Global Assessment; ITT, intention-to-treat; SE, standard error; SCORAD, Scoring of Atopic Dermatitis; TCS, topical corticosteroid.

Figure 3. Percentage improvement from baseline in pruritus NRS (A) for the ITT population.

*Nominal $p < 0.05$ for the comparison with placebo.

ITT, intention-to-treat; NRS, numerical rating scale; SE, standard error; TCS, topical corticosteroid.

429 **Tables**430 **Table 1.** Patient demographics and baseline disease characteristics.

	Placebo plus TCS (N = 56)	Tezepelumab 280 mg plus TCS (N = 55)
Age, years, mean (SD)	38.82 (15.28)	38.55 (14.92)
Male, n (%)	30 (53.6)	32 (58.2)
Race, n (%)		
White	42 (75.0)	49 (89.1)
Asian	5 (8.9)	2 (3.6)
Black or African-American	3 (5.4)	2 (3.6)
Native Hawaiian or other Pacific Islander	1 (1.8)	0
Other	2 (3.6)	1 (1.8)
Multiple categories checked	3 (5.4)	1 (1.8)
EASI score, mean (SD)	24.48 (11.21)	24.05 (12.38)
IGA classification, n (%) ^a		
Mild	0	1 (1.8)
Moderate	46 (82.1)	44 (80.0)
Severe	10 (17.9)	10 (18.2)
SCORAD, mean (SD)	58.66 (13.32)	57.68 (14.80)
Pruritus NRS, mean (SD)	5.2 (2.1)	5.3 (2.0)
Peak Pruritus, mean (SD)	6.2 (2.2)	6.4 (2.1)
Total serum IgE, kU/L, mean (SD)	9930.4 (16,583.5)	7550.3 (9334.1)
≥150 kU/L, n (%)	52 (92.9)	48 (87.3)
Positive <i>S. aureus</i> , n (%)		
Lesional skin	28 (57.1)	32 (66.7)
Non-lesional skin	18 (36.7)	18 (38.3)
Peripheral eosinophil count, cells/μL, mean	496.61 (381.42)	408.36 (256.39)

(SD)

≥300 cells/μL, n (%)	33 (58.9)	35 (63.6)
TCS use at screening, n (%)		
Low potency	2 (4.3)	2 (4.3)
Medium to high potency	45 (95.7)	44 (95.7)
Childhood AD, n (%)	46 (82.1)	48 (87.3)
Childhood asthma, n (%)	27 (48.2)	21 (38.2)
Adult asthma, n (%)	21 (38.2)	23 (44.2)

431 ^aIGA severity categories are 0 (clear), 1 (almost clear), 2 (mild), 3 (moderate), 4 (severe),
 432 and 5 (very severe).

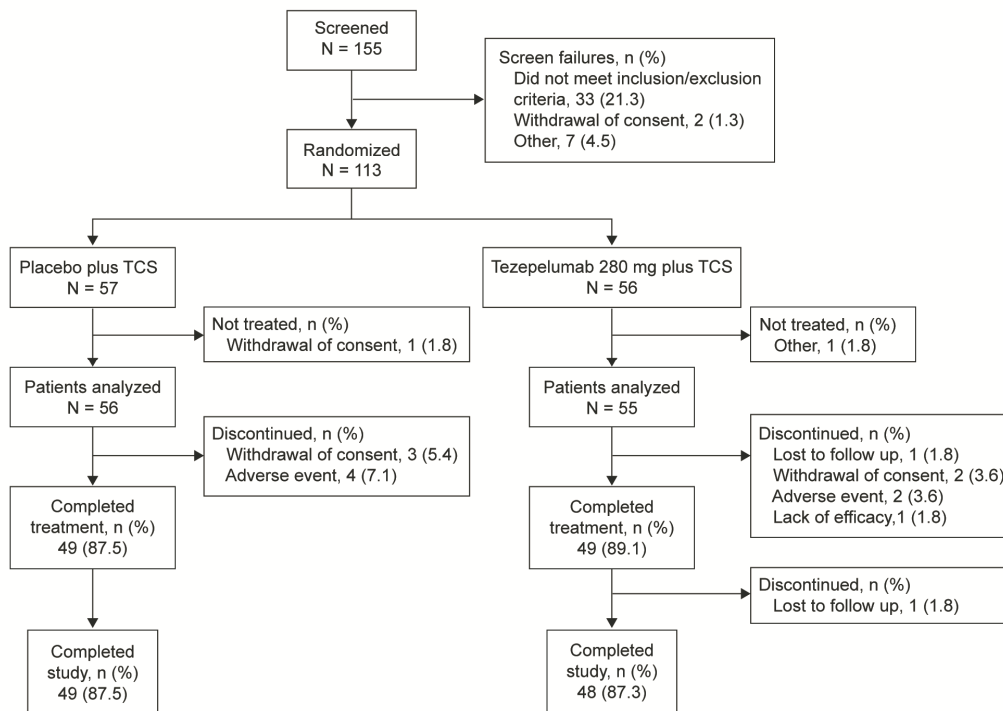
433 EASI, Eczema Area Severity Index; IGA, Investigator's Global Assessment; IgE,
 434 immunoglobulin E; NRS, numeric rating scale; *S. aureus*, *Staphylococcus aureus*; SCORAD,
 435 Scoring of Atopic Dermatitis; SD, standard deviation; TCS, topical corticosteroid.

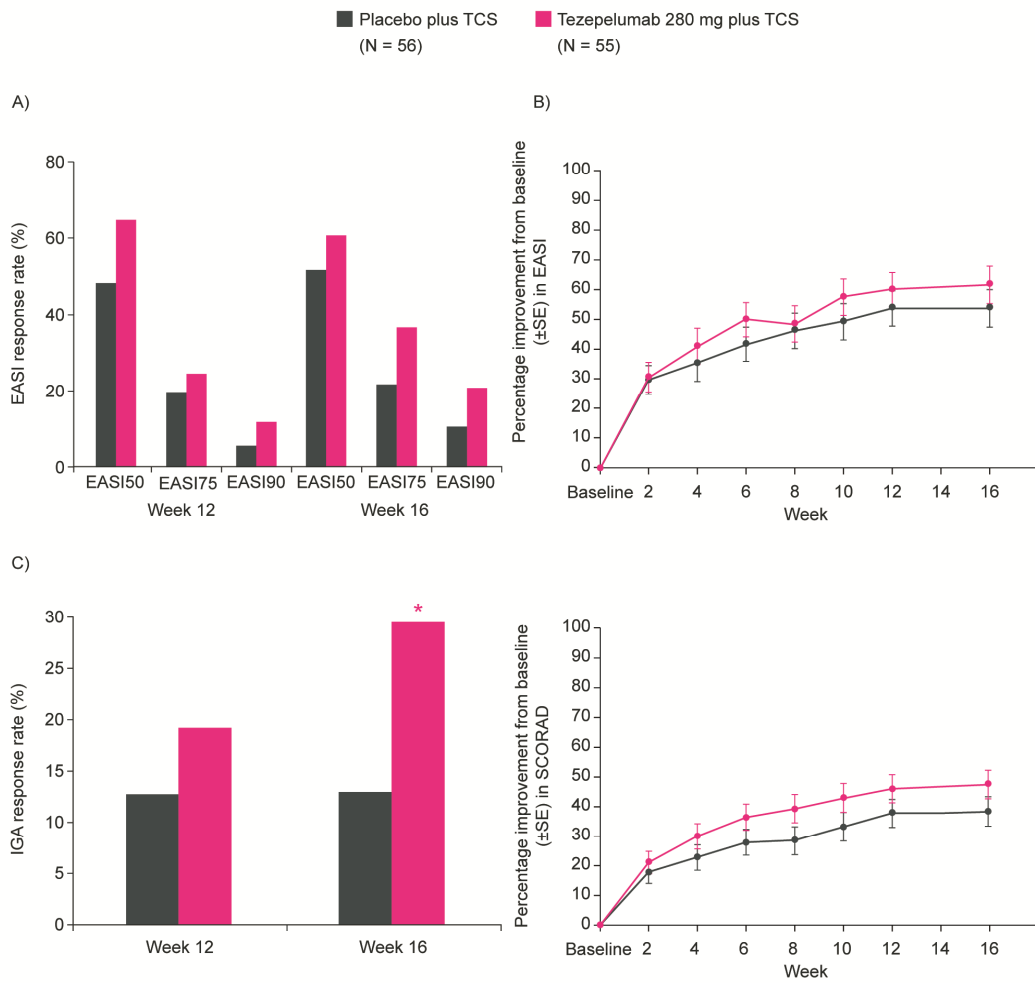
436 **Table 2.** Summary of treatment-emergent adverse events.

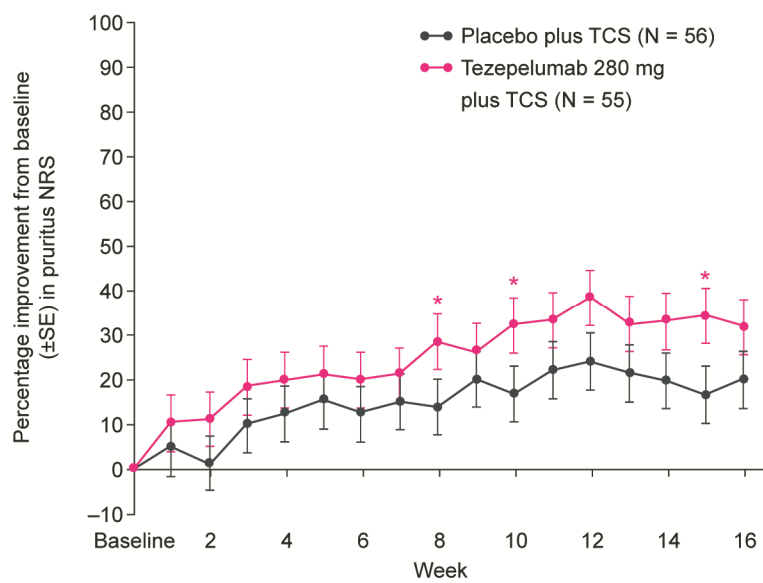
	Placebo plus TCS (N = 55)	Tezepelumab 280 mg plus TCS (N = 56)
At least one TEAE, n (%)	40 (72.7)	38 (67.9)
At least one treatment-related TEAE, n (%)	3 (5.5)	9 (16.1)
At least one TEAE leading to discontinuation, n (%)	4 (7.3)	2 (3.6)
At least one TESAE, n (%)	3 (5.5)	2 (3.6)
At least one treatment-related TESAE, n (%)	1 (1.8)	0
Death, n (%)	0	0
Most common TEAEs, occurring in $\geq 5\%$ of either treatment group, n (%)		
Nasopharyngitis	11 (20.0)	13 (23.2)
Atopic dermatitis	7 (12.7)	6 (10.7)
Upper respiratory tract infection	7 (12.7)	1 (1.8)
Diarrhea	3 (5.5)	5 (8.9)
Cellulitis	3 (5.5)	0
Headache	1 (1.8)	3 (5.4)
Injection-site erythema	0	3 (5.4)
Most common TESAEs, occurring in $\geq 1\%$ of either treatment group, n (%)		
Atopic dermatitis	1 (1.8)	1 (1.8)
Cellulitis	1 (1.8)	0
Chest pain	1 (1.8)	0
Infected dermal cyst	0	1 (1.8)
Syncope	1 (1.8)	0

437 TCS, topical corticosteroid; TEAE, treatment-emergent adverse event; TESAE,

438 treatment-emergent serious adverse event.







1 CAPSULE SUMMARY

- 2 • Thymic stromal lymphopoietin may initiate inflammation and therefore be a key
3 target for atopic dermatitis treatment
- 4 • Here, thymic stromal lymphopoietin blockade shows limited efficacy after 12 weeks'
5 treatment; findings at later time points suggest that future clinical trials may require
6 longer treatment periods to determine a significant treatment effect

ACCEPTED MANUSCRIPT