Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. List of Investigators

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eMethods

Protocol Amendments and Rationale

Amendments made to the trial protocol after trial commencement are summarized in **eTable 3**.

Analysis of Exploratory Efficacy End Points

Exploratory efficacy end points included:

- proportion of patients achieving ≥50% improvement in psoriasis area and severity index (PASI) score from baseline (PASI 50) at weeks 2, 4, 8, and 12
- proportion of patients achieving ≥75% improvement in PASI score from baseline (PASI 75) at weeks 2, 4, and 8
- proportion of patients achieving ≥90% improvement in PASI score from baseline (PASI 90) at weeks 2, 4, and 8
- proportion of patients achieving 100% improvement in PASI score from baseline (PASI 100) at weeks 2, 4 and 8
- change from baseline in PASI score at weeks 2, 4, 8, and 12
- percent change from baseline in PASI score at weeks 2, 4, ,8 and 12
- change from baseline in Physician's Global Assessment (PGA) score at weeks 2, 4, 8, and 12
- proportion of patients achieving a PGA score of clear (0) or almost clear (1) at weeks 2, 4, and 8
- proportion of patients with at least a 2-grade decrease from baseline in PGA score at weeks 2, 4, 8, and 12
- change from baseline in affected body surface area (BSA) at weeks 2, 4, 8, and 12
- change from baseline in pruritus Numerical Rating Scale (NRS) at weeks 2, 4, 8, and 12
- proportion of patients with a baseline pruritus NRS of 4 or greater achieving a ≥4 point decrease from baseline at weeks 2, 4, 8, and 12
- change from baseline in Dermatology Life Quality Index (DLQI) at weeks 4 and 8
- change from baseline in pain NRS at weeks 2, 4, 8, and 12 for patients with concomitant psoriatic arthritis.

Exploratory endpoints involving proportions of patients were analyzed using a Cochran–Mantel–Haenszel test (using previous biologic treatment as a stratification factor) to compare responses between each active treatment group and placebo. Continuous exploratory end points involving change from baseline were analyzed using a mixed model for repeated measures method, including treatment group, visit (weeks 2, 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as a covariate.

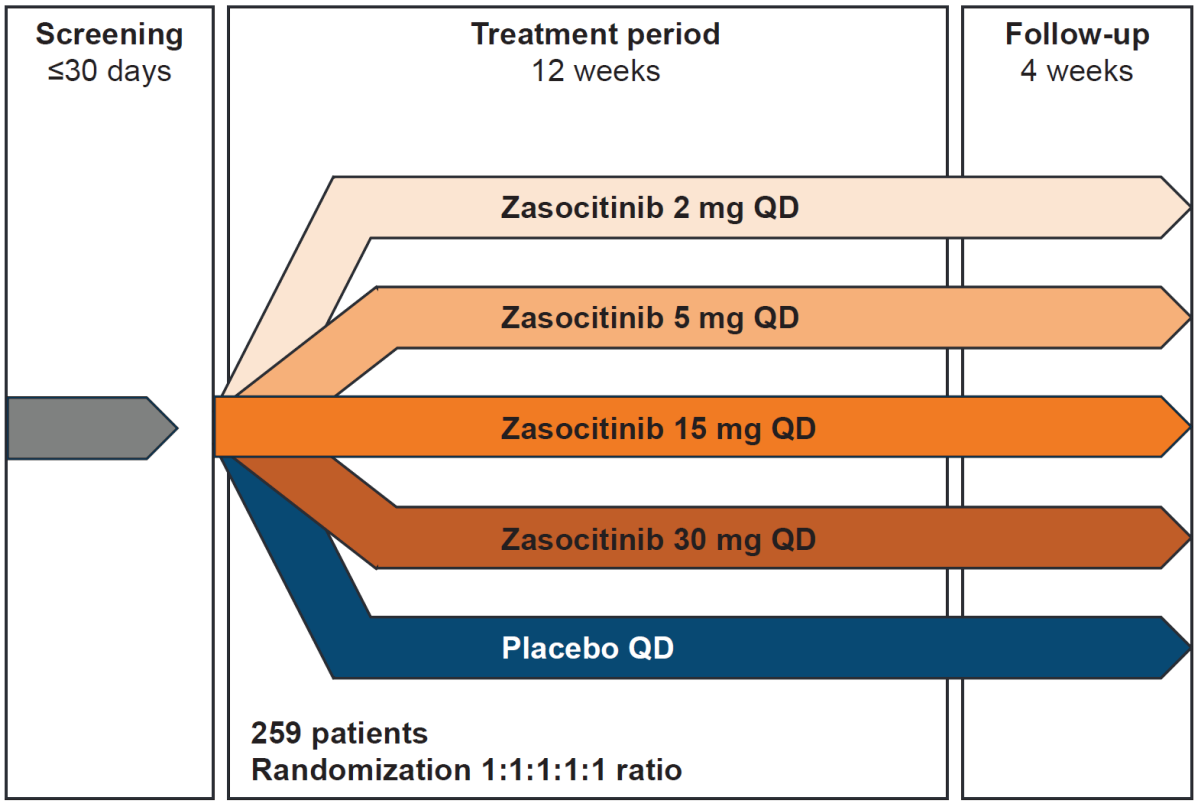
eResults

Exploratory Efficacy Outcomes

A greater change from baseline in affected BSA was observed with zasocitinib 15 and 30 mg compared with placebo at week 2, which was maintained up to week 12 (**eFigure 3**). A greater difference was observed at weeks 8 and 12 with zasocitinib 5 mg while no differences were observed at any visits for the lowest dose (2 mg) (**eFigure 3**). In total, 53 patients (21%) achieved a BSA ≤1% at week 12. A greater change from baseline in affected BSA ≤1% was observed with zasocitinib 5 mg than with placebo at week 12, and 15 and 30 mg compared with placebo at week 8, which was maintained up to week 12 (**eFigure 12**).

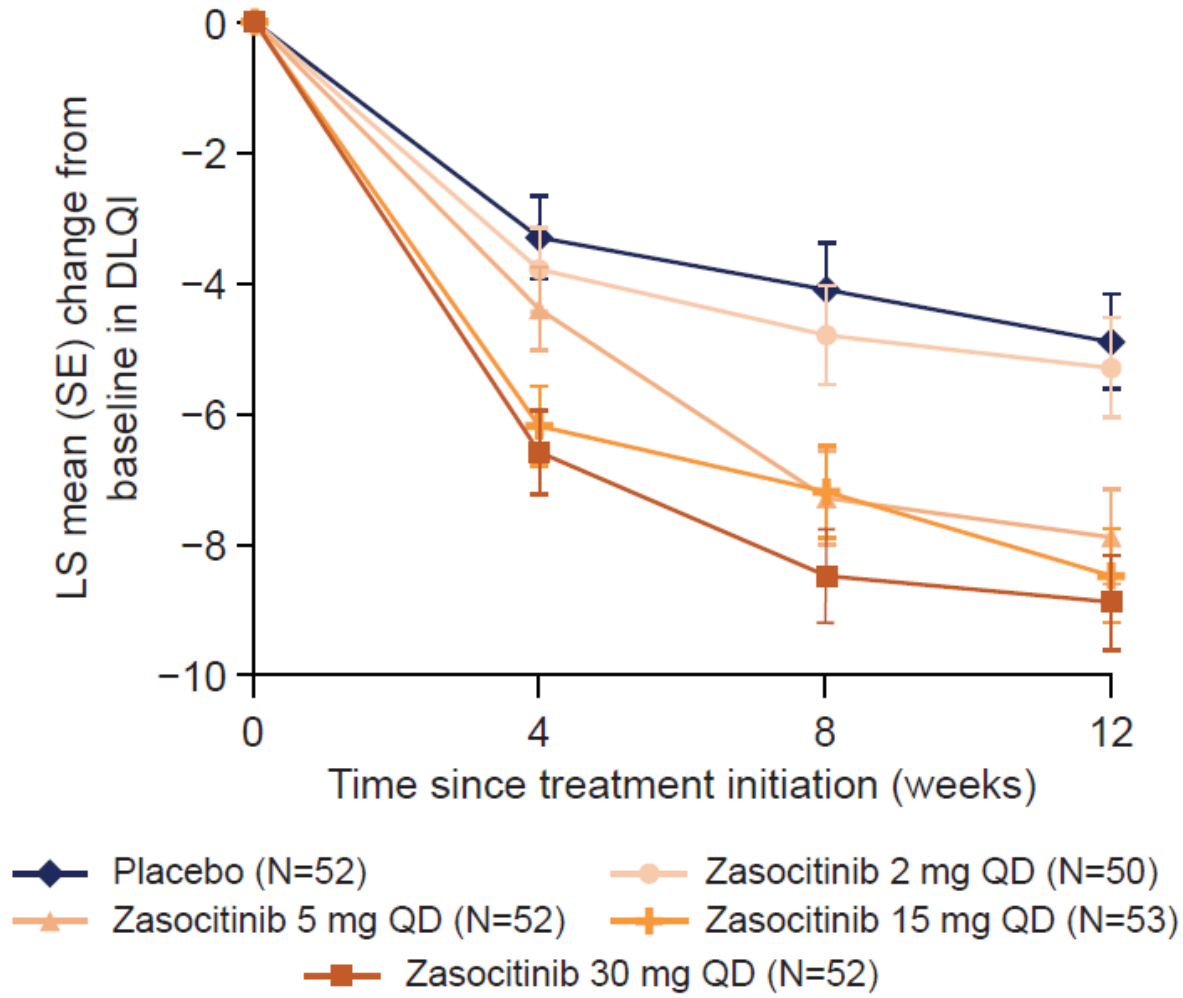
PASI 50 was achieved at week 12 in 40%, 65%, 79%, and 77% of patients in the zasocitinib 2, 5, 15 and 30 mg groups, respectively, and in 25% of patients receiving placebo, with differences apparent as early as week 2 (**eFigure 4**). A greater change from baseline in PASI was observed in patients receiving zasocitinib 5, 15, and 30 mg QD than among patients receiving placebo, with differences also apparent as early as week 2 (**eFigure 5**). Similar results were observed for percentage change from baseline in PASI (**eFigure 6**). Change from baseline in PGA was most pronounced in patients receiving zasocitinib 15 and 30 mg, although differences from placebo were observed in all treatment groups (**eFigure 7**). A total of 12%, 35%, 59%, and 56% of patients in the zasocitinib 2, 5, 15 and 30 mg groups, respectively, achieved a ≥2-grade reduction in PGA from baseline at week 12, relative to 4% of those receiving placebo (**eFigure 8**). Greater change from baseline in pruritus NRS was observed in patients receiving zasocitinib 15 and 30 mg than among patients receiving placebo (**eFigure 9**). Among patients with a baseline pruritus NRS score ≥4, a total of 49%, 55%, 66%, and 68% of patients receiving zasocitinib 2, 5, 15, and 30 mg, respectively, achieved a ≥4-point reduction in pruritus NRS at week 12, relative to 35% of patients receiving placebo (**eFigure 10**). Among patients with concomitant psoriatic arthritis, change from baseline in pain NRS was greatest among patients receiving zasocitinib 30 mg, although it should be noted that patient numbers for this analysis were very low (n = 3, 3, 8, 6, and 5 for patients receiving placebo and zasocitinib 2, 5, 15, and 30 mg, respectively) **(eFigure 11**). A total of 21%, 29%, 59% and 45% of patients receiving zasocitinib 2, 5, 15, and 30 mg, respectively, achieved a DLQI of 0 or 1 at week 12, versus 16% or those receiving placebo (**eTable 2**)

eFigure 1. Design of Phase 2b Study of Zasocitinib in Patients With Moderate-to-Severe Plaque Psoriasis



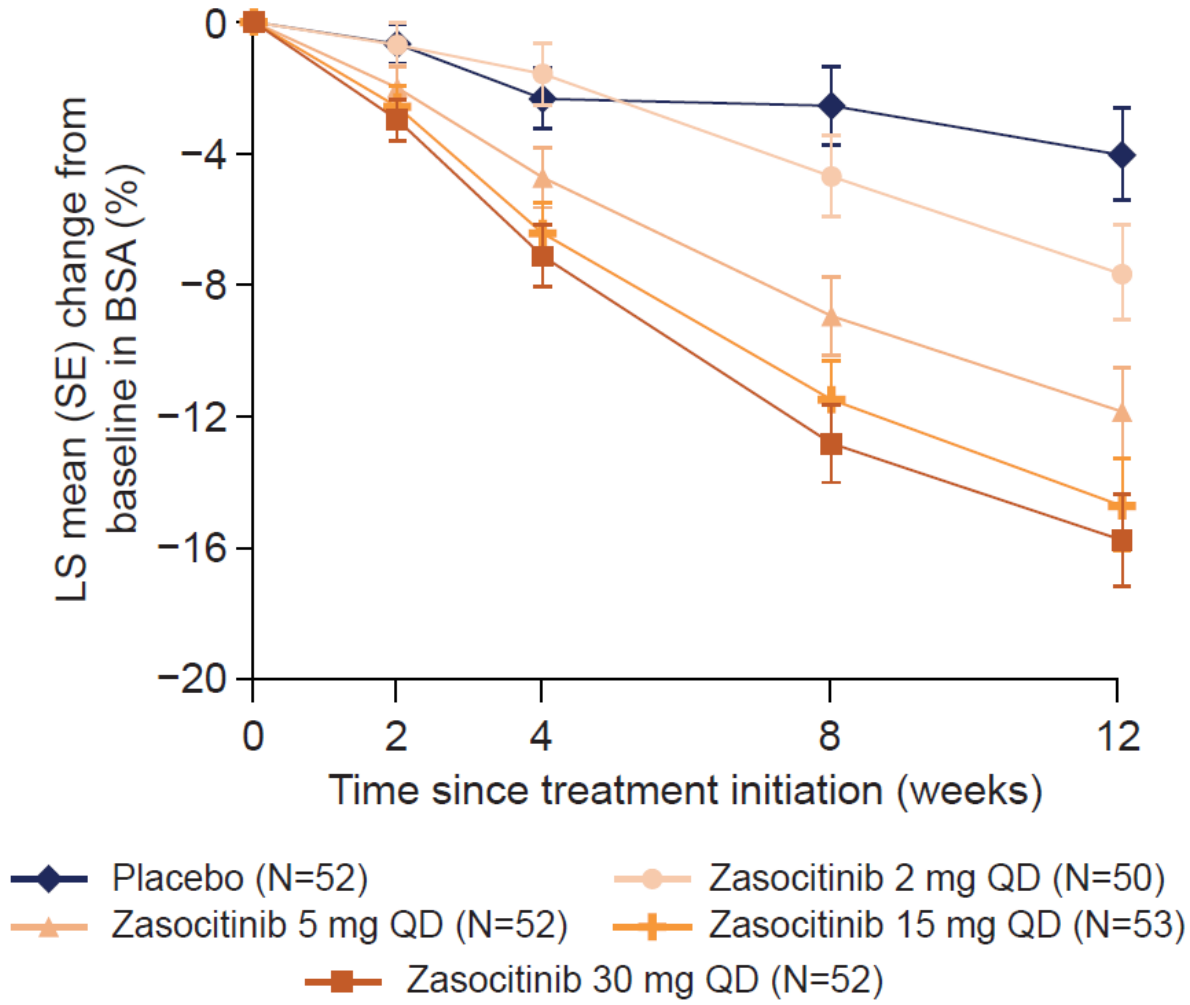
QD, once daily.

eFigure 2. Change from Baseline in DLQI in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



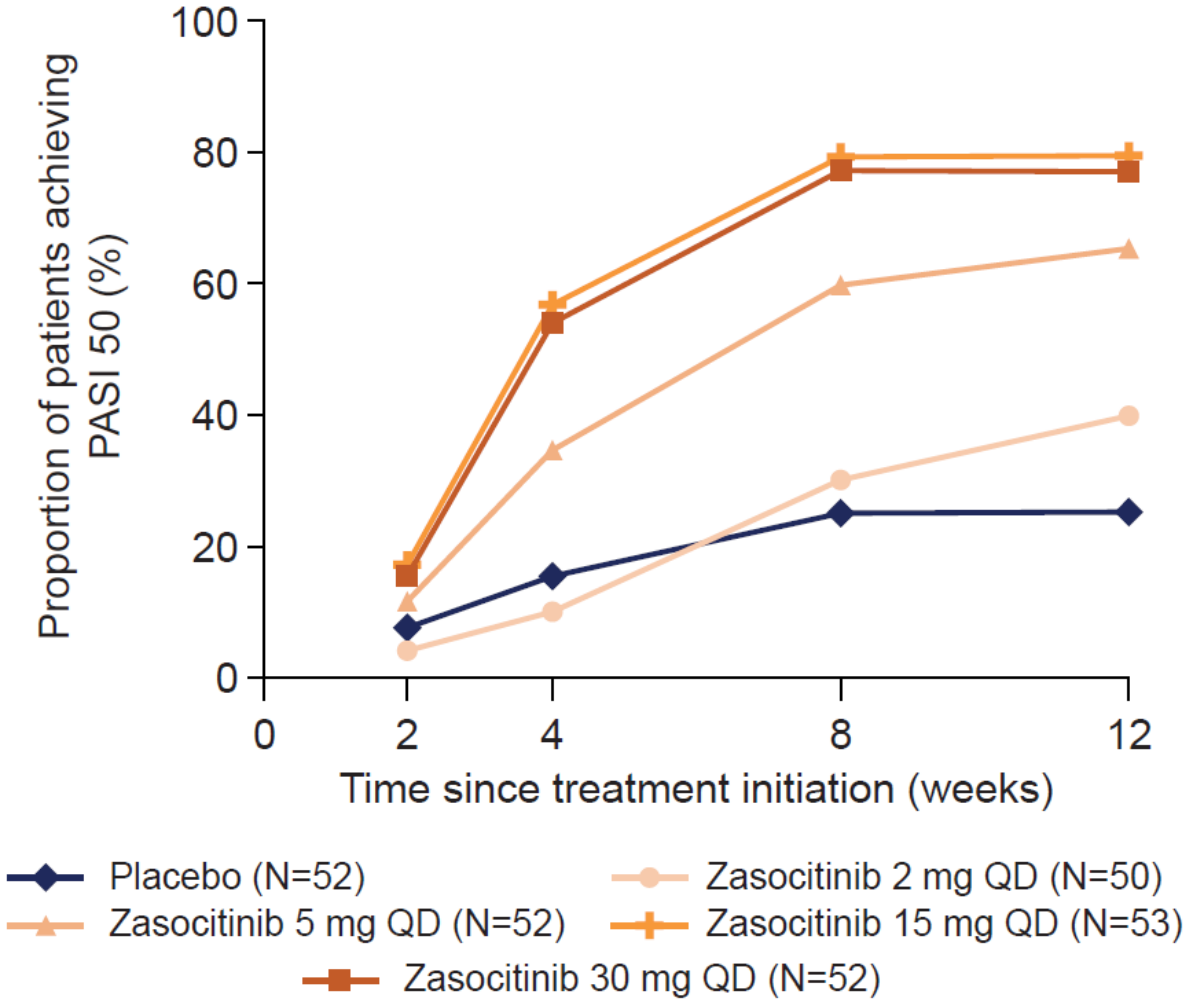
Lower DLQI scores indicate greater quality of life. LS means and SE were from a mixed model for repeated measures on the change from baseline in DLQI. The model included treatment, visit (weeks 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as covariate. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with assessments collected on the day of or after the start of a prohibited medication that was considered as major protocol deviation were set as missing. DLQI, Dermatology Life Quality Index; LS, least-squares; mITT, modified intent-to-treat; QD, once daily; SE, standard error.

eFigure 3. Change from Baseline in BSA Affected by Psoriasis in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



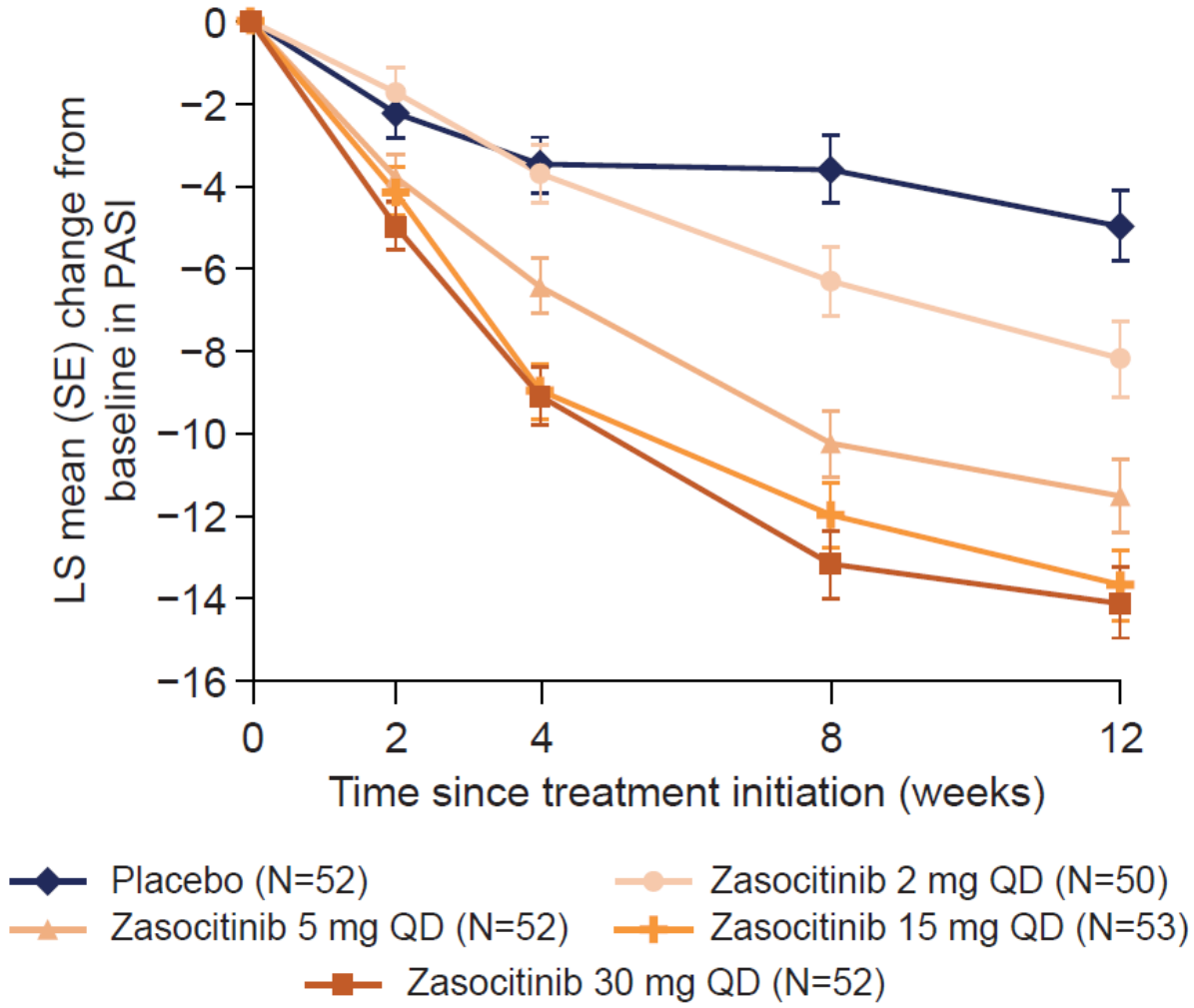
LS means and SE were from a mixed model for repeated measures on the change from baseline in BSA. The model included treatment, visit (weeks 2, 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as covariate. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with assessments collected on the day of or after the start of a prohibited medication that was considered as major protocol deviation were set as missing. BSA, body surface area; LS, least-squares; mITT, modified intent-to-treat; QD, once daily; SE, standard error.

eFigure 4. Time Course of PASI 50 Response Rates In Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



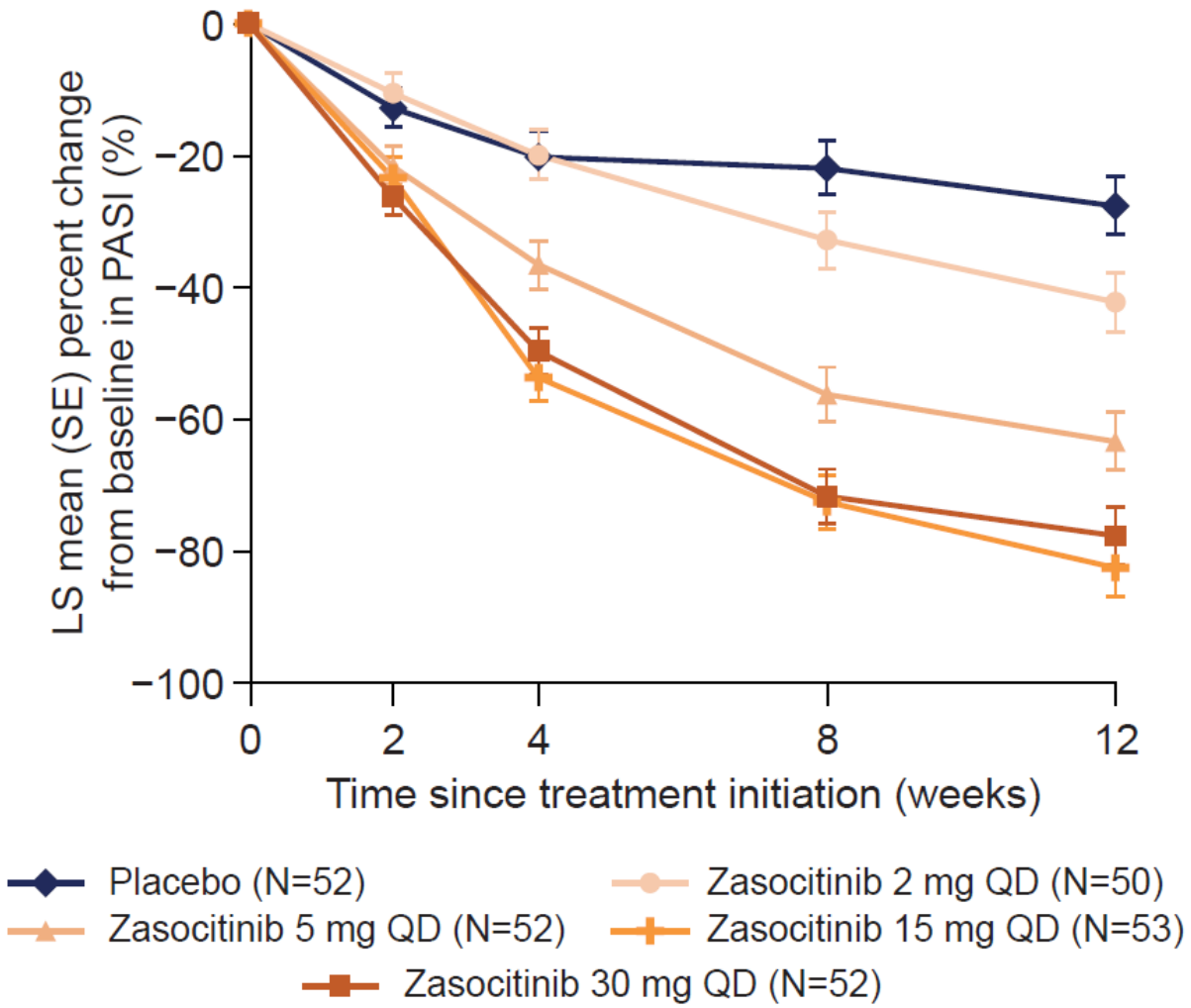
Patients with missing values were imputed as non-responders. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were imputed as non-responders. mITT, modified intent-to-treat; PASI, psoriasis area and severity index; QD, once daily.

eFigure 5. Change from Baseline in PASI in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



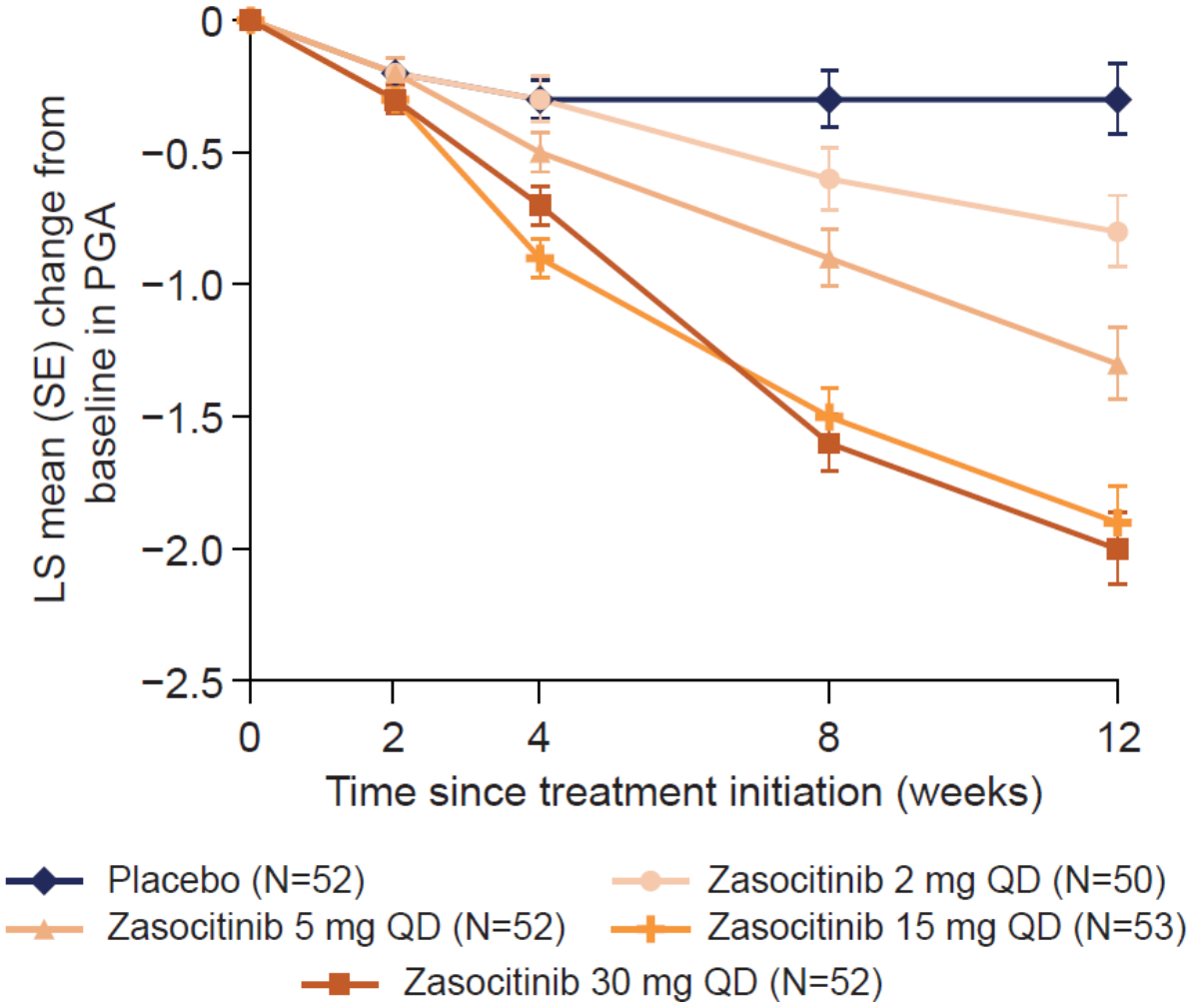
LS means and SE were from a mixed model for repeated measures on the change from baseline in PASI. The model included treatment, visit (weeks 2, 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as covariate. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were set as missing. LS, least-squares; mITT, modified intent-to-treat; PASI, psoriasis area and severity index; QD, once daily; SE, standard error.

eFigure 6. Percent Change from Baseline in PASI in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



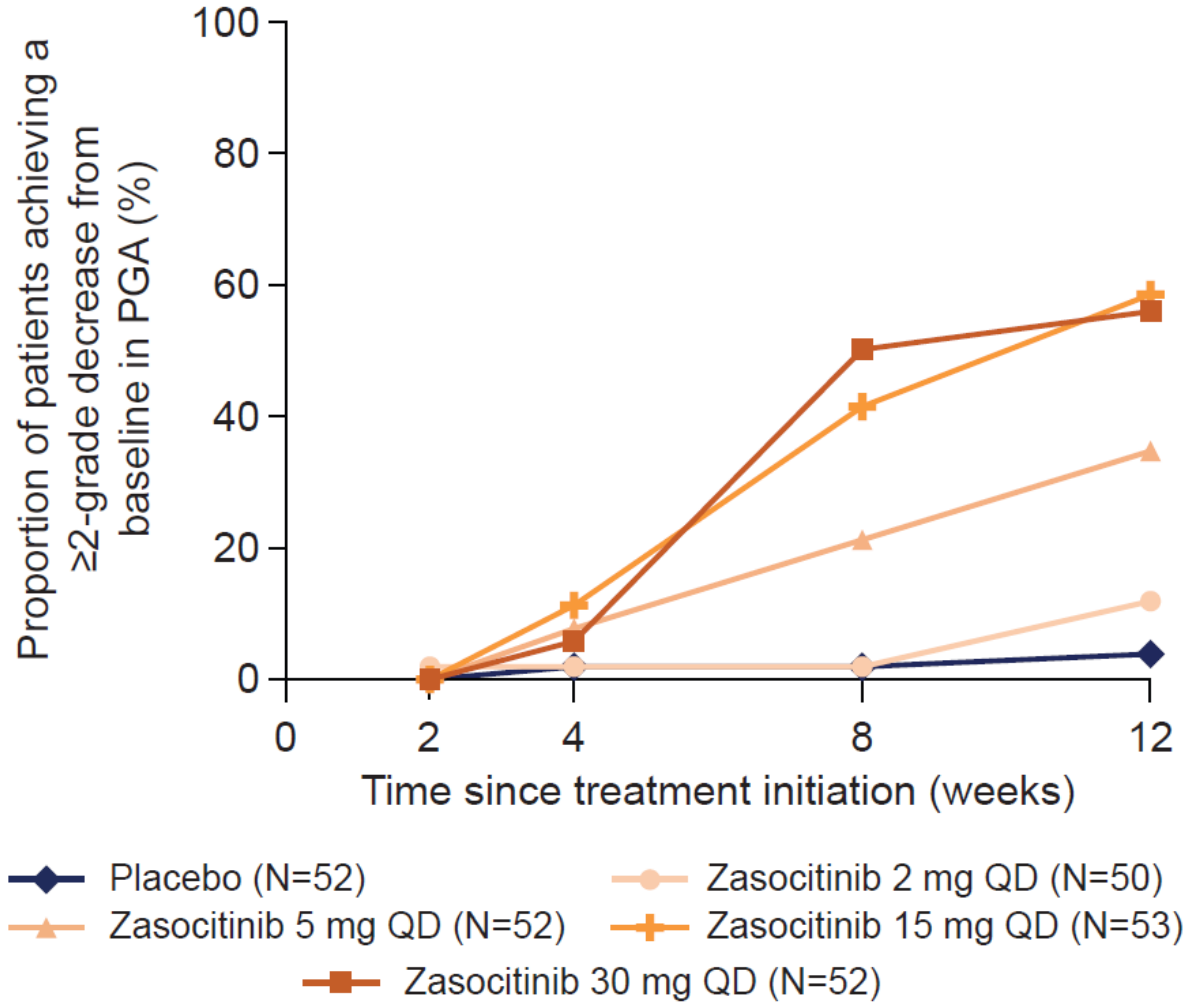
LS means and SE were from a mixed model for repeated measures on the percent change from baseline in PASI. The model included treatment, visit (weeks 2, 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as covariate. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were set as missing. LS, least-squares; mITT, modified intent-to-treat; PASI, psoriasis area and severity index; QD, once daily; SE, standard error.

eFigure 7. Change from Baseline in PGA in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



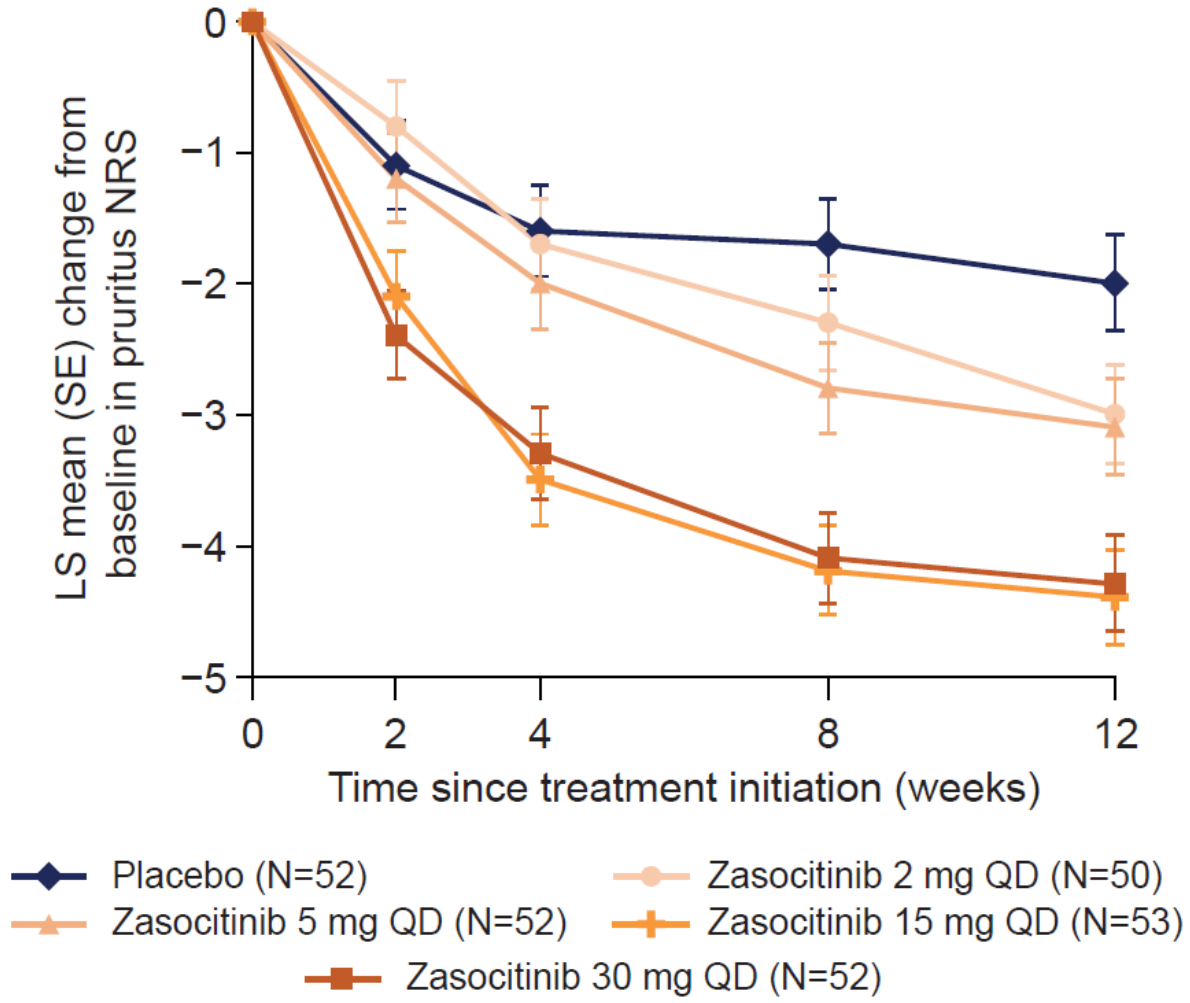
LS means and SE were from a mixed model for repeated measures on the change from baseline in PGA. The model included treatment, visit (weeks 2, 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as covariate. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were set as missing. LS, least-squares; mITT, modified intent-to-treat; PGA, Physician's Global Assessment; QD, once daily; SE, standard error.

eFigure 8. Proportion of Patients Achieving a ≥2-Grade Decrease from Baseline in PGA at Weeks 2, 4, 8, and 12 in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



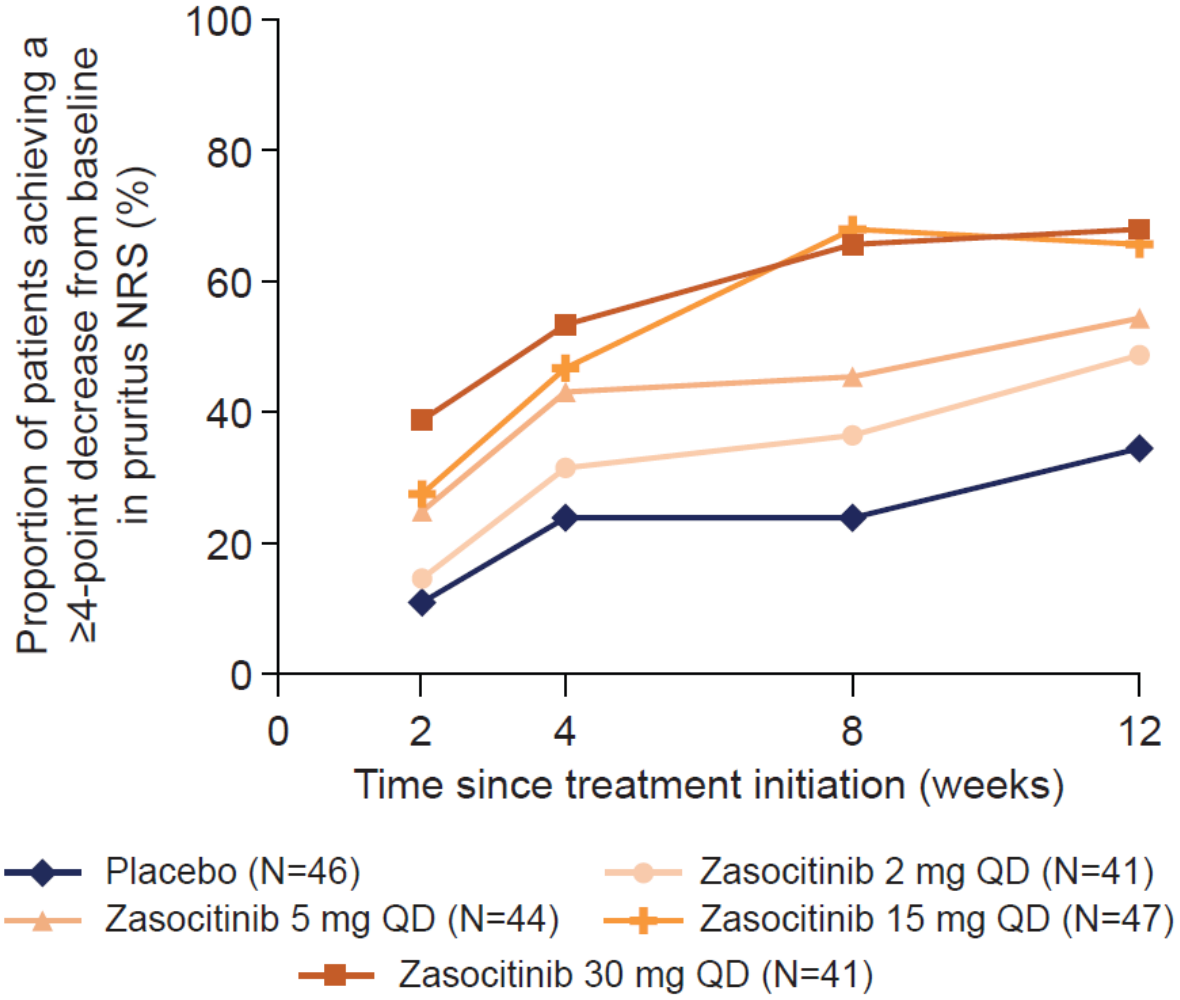
Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with missing values were imputed as non-responders. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were imputed as non-responders. mITT, modified intent-to-treat; PGA, Physician's Global Assessment; QD, once daily.

eFigure 9. Change from Baseline in Pruritus NRS in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



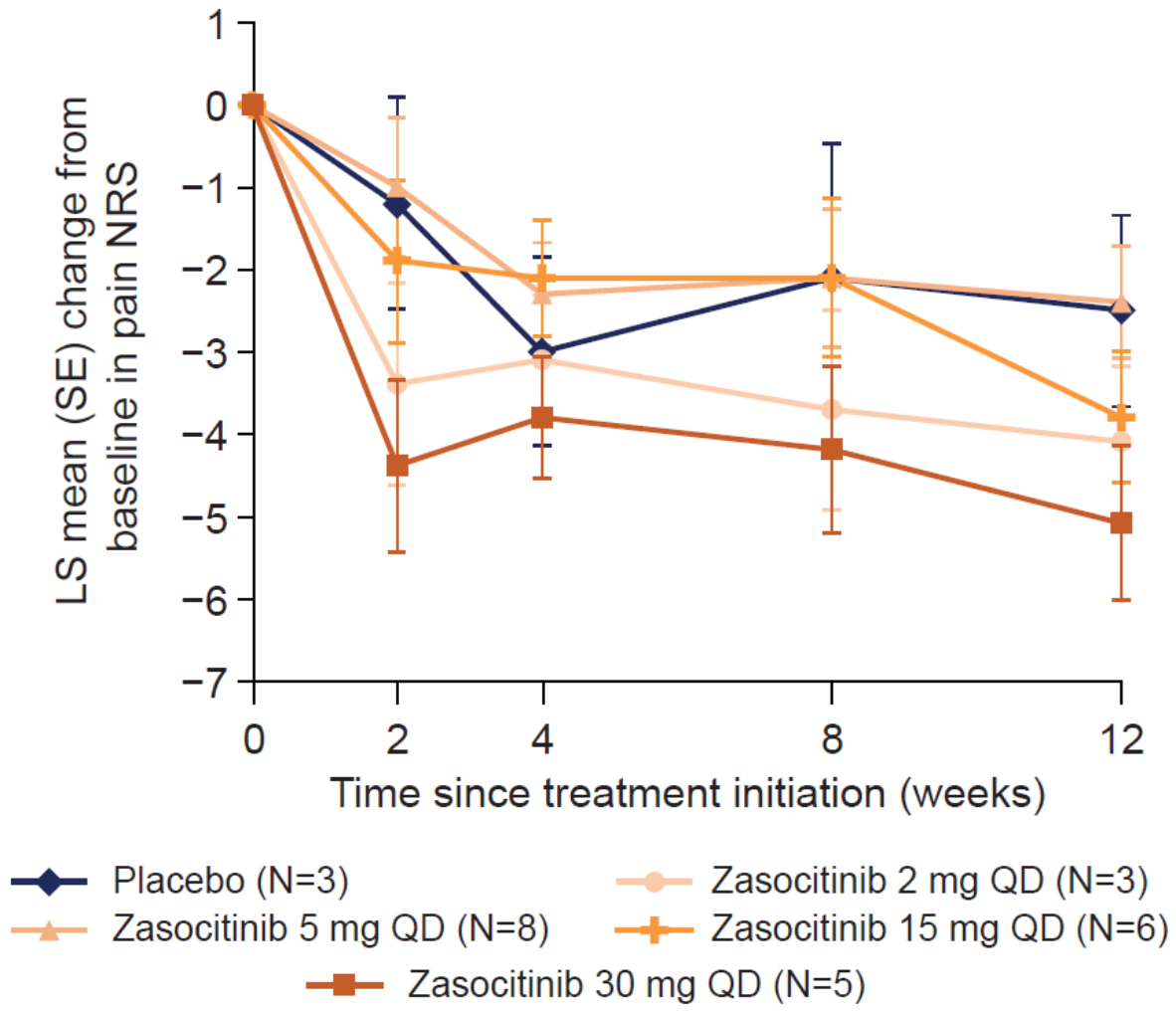
LS means and SE were from a mixed model for repeated measures on the change from baseline in pruritus NRS. The model included treatment, visit (weeks 2, 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as covariate. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were set as missing. LS, least-squares; mITT, modified intent-to-treat; NRS, numerical rating scale; QD, once daily; SE, standard error.

eFigure 10. Proportion of Patients with a Baseline Pruritus NRS Score of ≥4 Achieving a ≥4-Point Decrease from Baseline at Weeks 2, 4, 8, and 12 in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study of Zasocitinib (mITT Analysis Set)



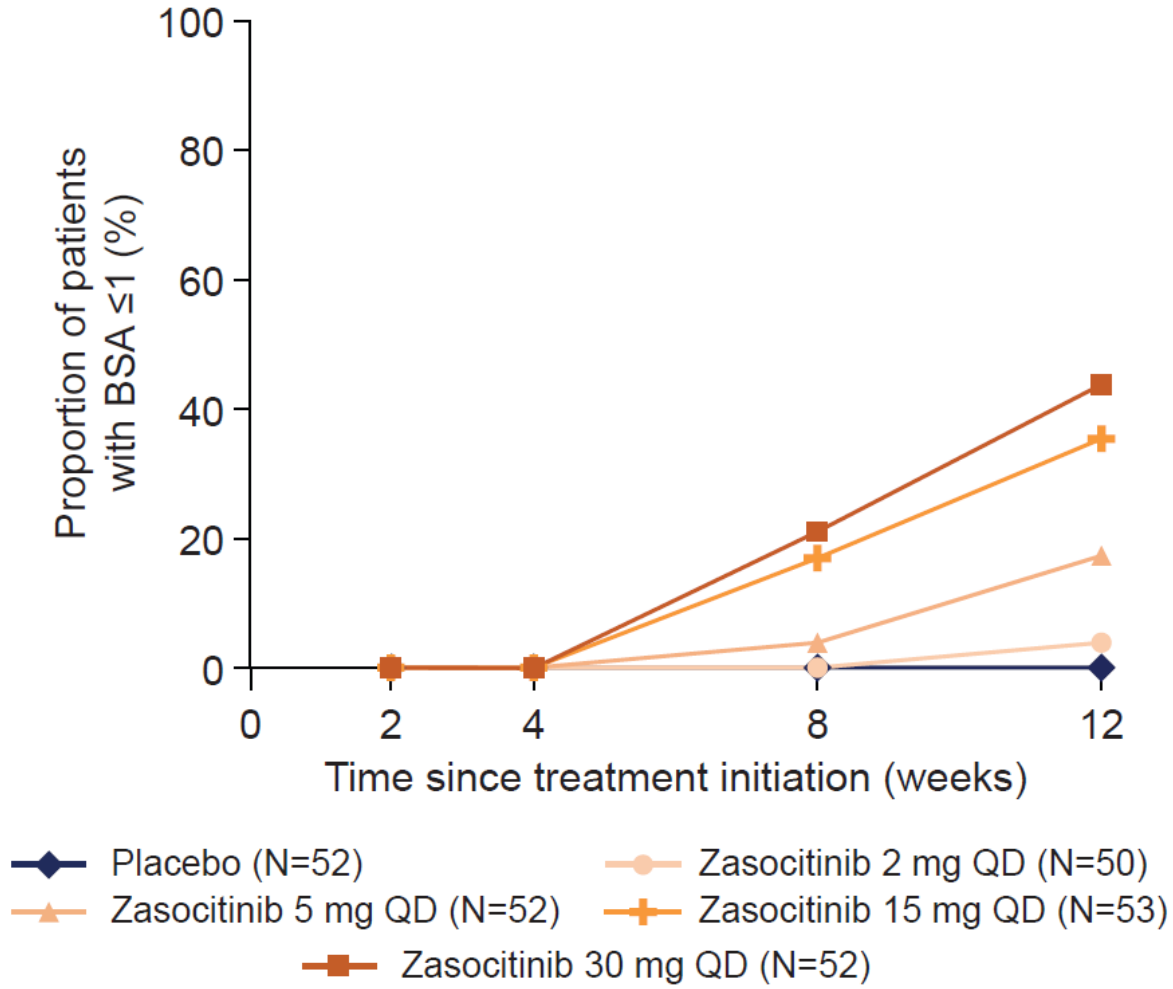
Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Percentages are based on the number of patients with a result at the specified visit and with a baseline pruritus NRS of ≥4 in each treatment group. Patients with missing values were imputed as non-responders, for patients with a baseline pruritus NRS of ≥4. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were imputed as non-responders. mITT, modified intent-to-treat; NRS, numerical rating scale; QD, once daily.

eFigure 11. Change from Baseline in Pain NRS Among Patients with Concomitant Psoriatic Arthritis, in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study for Zasocitinib (mITT Analysis Set)



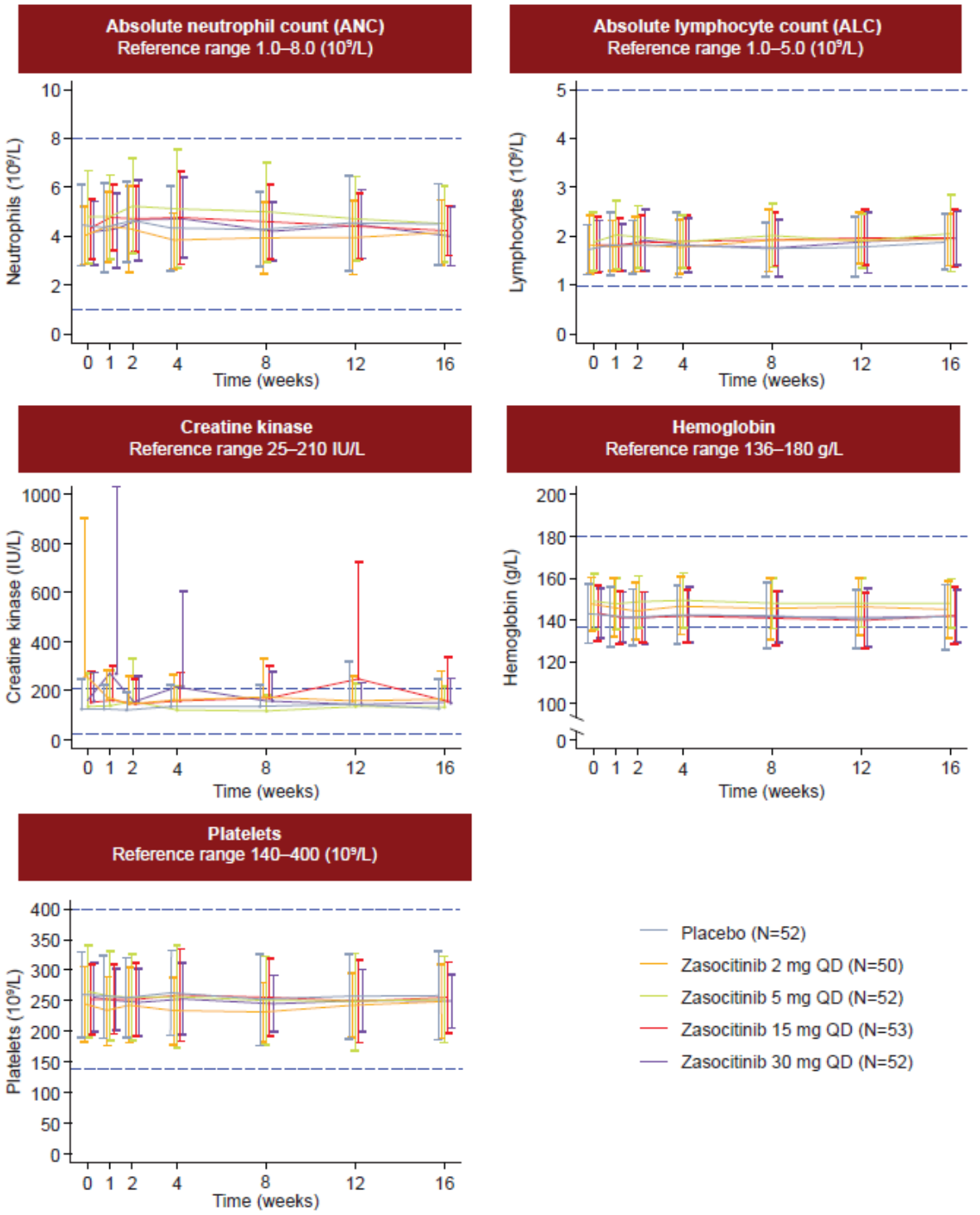
LS means and SE were from a mixed model for repeated measures on the change from baseline in pain NRS. The model included treatment, visit (weeks 2, 4, 8, and 12), treatment-by-visit interaction, and previous treatment with biologics as fixed effects and baseline score as covariate. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise. Patients with assessments collected on the day of, or after the start of, a prohibited medication that was considered as major protocol deviation were set as missing. LS, least-squares; mITT, modified intent-to-treat; NRS, numerical rating scale; QD, once daily; SE, standard error.

eFigure 12. Time Course of Affected BSA ≤1% Response in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study for Zasocitinib (mITT Analysis Set)



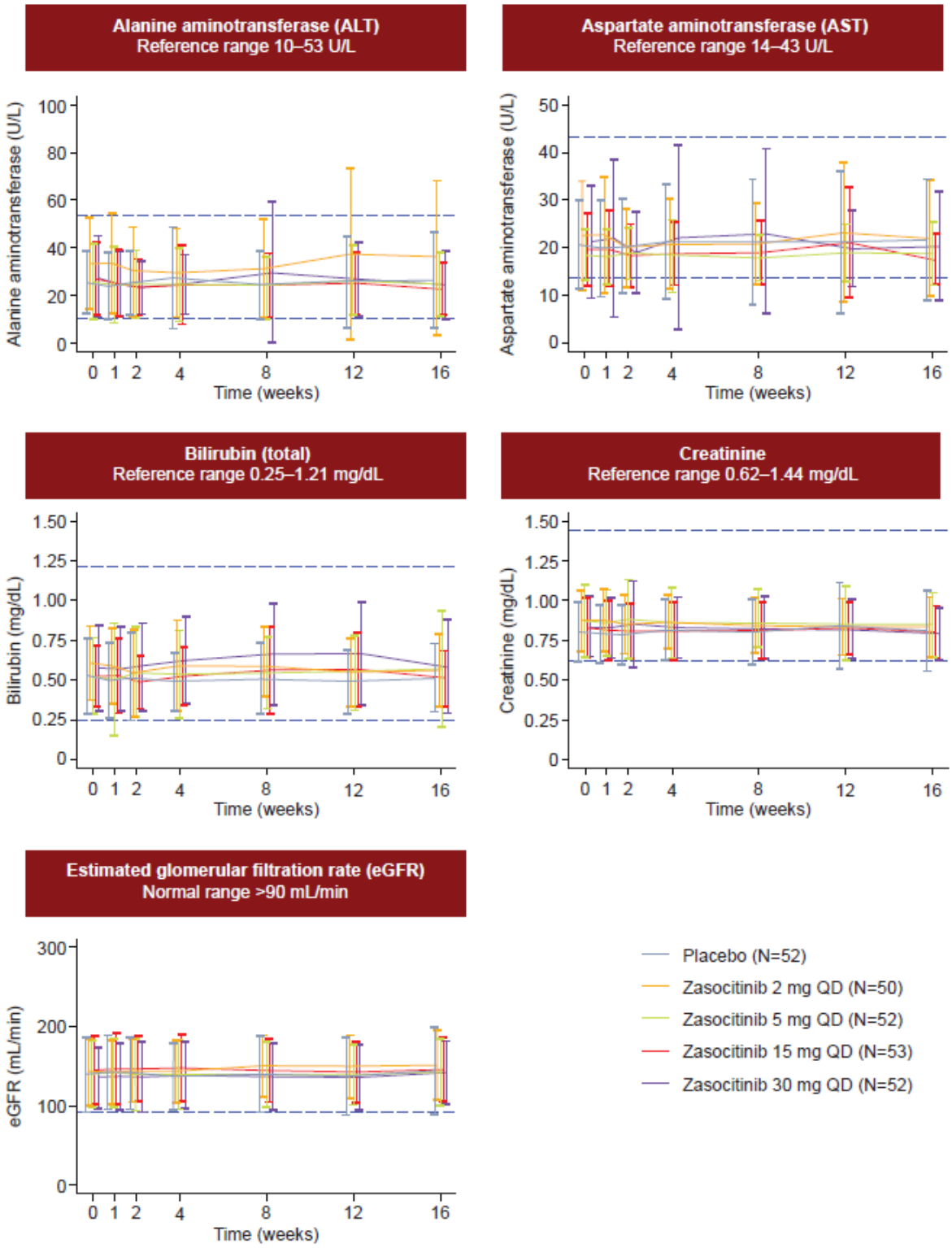
These data are derived from a *post hoc* analysis because affected BSA ≤1% was not a prespecified end point of the study. BSA, body surface area; mITT, modified intent-to-treat; QD, once daily.

eFigure 13. Change from Baseline in Hematologic Parameters and Creatine Kinase in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study for Zasocitinib (Safety Analysis Set)



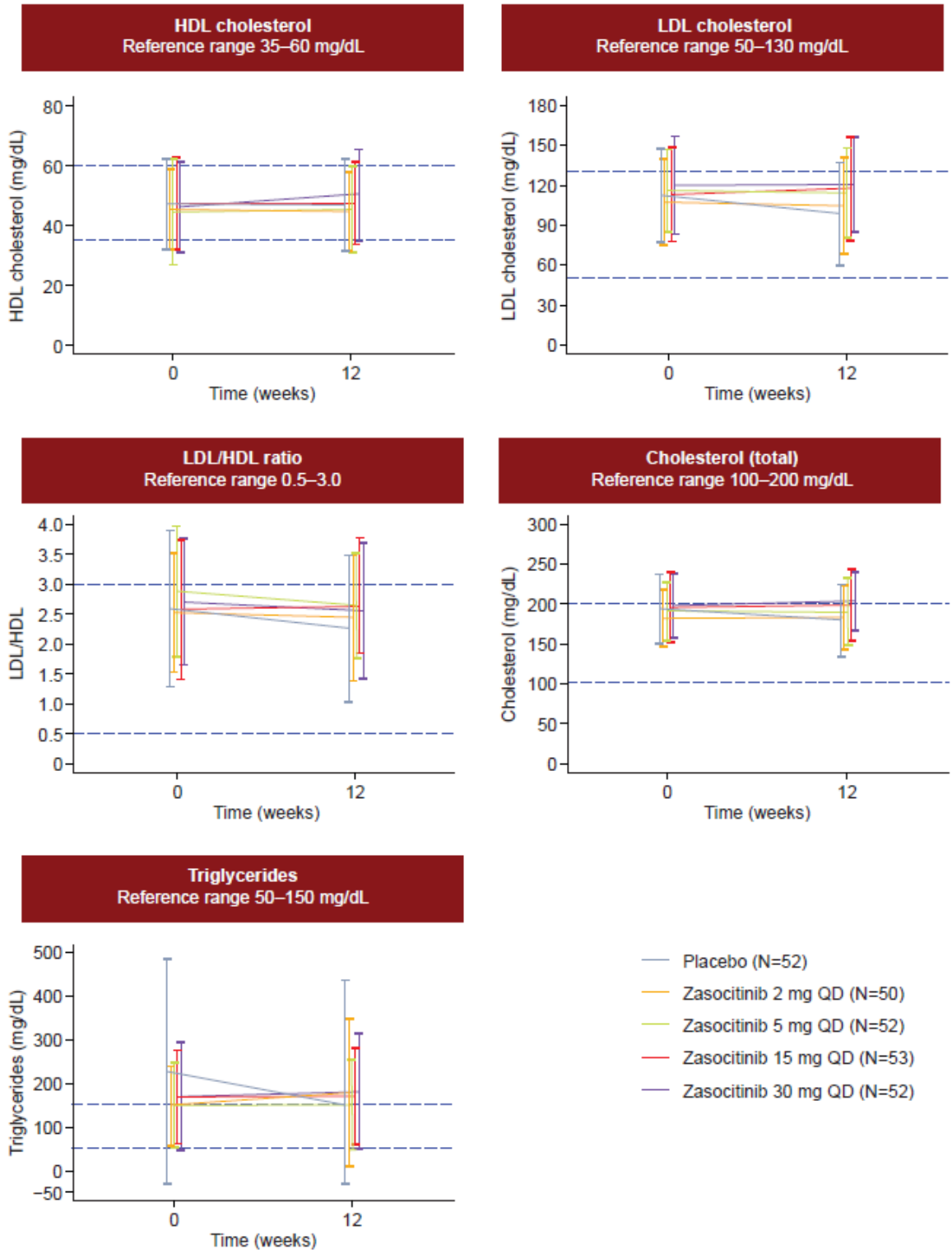
Data represent mean ± standard deviation. Due to the large variability in the creatine kinase values, one-sided error bars are shown for the creatine kinase graph. ALC, absolute lymphocyte count; ANC, absolute neutrophil count; QD, once daily.

eFigure 14. Change from Baseline in Hepatic and Renal Parameters in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study for Zasocitinib (Safety Analysis Set)



Data represent mean ± standard deviation. ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; QD, once daily.

eFigure 15. Change from Baseline in Lipid Parameters in Patients With Moderate-to-Severe Psoriasis in a Phase 2b Study for Zasocitinib (Safety Analysis Set)



Data represent mean ± standard deviation. HDL, high-density lipoprotein; LDL, low-density lipoprotein; QD, once daily.

eTable 1. Proportion of Patients With Moderate-to-Severe Psoriasis Receiving Zasocitinib Who Achieved PASI 75, 90, and 100 Responses at Weeks 2, 4, 8, and 12 (mITT Analysis Set)

End Point[a]	Placebo (n=52)	Zasocitinib 2 mg QD (n=50)	Zasocitinib 5 mg QD (n=52)	Zasocitinib 15 mg QD (n=53)	Zasocitinib 30 mg QD (n=52)
PASI 75 (primary end point)					
Week 2					
No. of patients (%)	0	0	1 (2)	0	2 (4)
Proportion difference vs. placebo, % (95% CI)[b]	–	0	2 (–2, 6)	0	4 (–1, 9)
Week 4					
No. of patients (%)	1 (2)	0	5 (10)	15 (28)	9 (17)
Proportion difference vs. placebo, % (95% CI)[b]	–	–2 (–6, 2)	8 (–1, 17)	26 (14, 39)	15 (4, 26)
Week 8					
No. of patients (%)	3 (6)	4 (8)	16 (31)	26 (49)	29 (56)
Proportion difference vs. placebo, % (95% CI)[b]	–	2 (–7, 12)	25 (11, 39)	43 (28, 58)	50 (35, 65)
Week 12 (primary end point)					
No. of patients (%)	3 (6)	9 (18)	23 (44)	36 (68)	35 (67)
P value vs. placebo	–	.052	<.001	<.001	<.001
Proportion difference vs. placebo, % (95% CI)[b]	–	12 (0, 25)	39 (24, 53)	62 (48, 76)	62 (47, 76)
PASI 90					
Week 2					
No. of patients (%)	0	0	1 (2)	0	0
Proportion difference vs. placebo, % (95% CI)[b]	–	–	2 (–2, 6)	–	–
Week 4					
No. of patients (%)	0	0	0	1 (2)	3 (6)
Proportion difference vs. placebo, % (95% CI)[b]	–	–	–	2 (–2, 5)	6 (–1, 12)
Week 8					
No. of patients (%)	0	0	5 (10)	13 (25)	17 (33)
Proportion difference vs. placebo, % (95% CI)[b]	–	–	10 (2, 18)	25 (13, 36)	33 (20, 45)
Week 12					
No. of patients (%)	0	4 (8)	11 (21)	24 (45)	24 (46)
Proportion difference vs. placebo, % (95% CI)[b]	–	8 (1, 16)	21 (10, 32)	45 (32, 59)	46 (33, 60)

PASI 100					
Week 2					
No. of patients (%)	0	0	0	0	0
Proportion difference vs. placebo, % (95% CI)[b]	–	–	–	–	–
Week 4					
No. of patients (%)	0	0	0	0	0
Proportion difference vs. placebo, % (95% CI)[b]	–	–	–	–	–
Week 8					
No. of patients (%)	0	0	0	5 (9)	5 (10)
Proportion difference vs. placebo, % (95% CI)[b]	–	–	–	9 (1, 17)	10 (2, 18)
Week 12					
No. of patients (%)	0	1 (2)	5 (10)	8 (15)	17 (33)
Proportion difference vs. placebo, % (95% CI)[b]	–	2 (–2, 6)	10 (2, 18)	15 (5, 25)	33 (20, 45)

Abbreviations: CI, confidence interval; CMH, Cochran–Mantel–Haenszel; MH, Mantel–Haenszel; mITT, modified intent-to-treat; NE, not evaluable; PASI, Psoriasis Area and Severity Index; QD, once daily.

Missing values were imputed as non-responders. Patients with assessments collected on the day of or after the start of a prohibited medication that was adjudicated as major protocol deviation were set as non-responders.

[a]The PASI is a composite score ranging from 0 to 72 that takes into account the degree of erythema, induration/infiltration, and desquamation (each scored from 0 to 4 separately) for each of four body regions, with adjustments for the percentage of the BSA involved for each body region and for the proportion of the body region to the whole body. For PASI calculation, the four main body regions were assessed: the head, the trunk, and the upper and lower extremities, corresponding to 10, 20, 30, and 40% of the total body area, respectively. The area of psoriatic involvement of these four main regions was given a numerical value: "0" indicating "no involvement" "1" indicating <10% psoriatic involvement, "2" indicating 10–<30% psoriatic involvement, "3" indicating 30–<50% psoriatic involvement, "4" indicating 50–<70% psoriatic involvement, "5" indicating 70–<90% psoriatic involvement, and "6" indicating 90–100% psoriatic involvement.[29]

[b]Proportion difference for achievement of PASI 75, PASI 90, and PASI 100 was calculated using the MH method. The *P* value for the primary end point was derived from a CMH test, with previous treatment with biologics included as a stratification factor, and compared the proportion of patients achieving PASI 75 in each dose group of zasocitinib versus placebo. *P* values for other end points are not reported because these values have not been adjusted for multiple comparisons; 95% CIs are unadjusted. PASI 75, PASI 90, and PASI 100 were defined as at least 75%, 90%, and 100% reduction from baseline in PASI, respectively. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time is available, and before or on the first study treatment dosing date otherwise.

eTable 2. Proportion of Patients With Moderate-to-Severe Psoriasis Receiving Zasocitinib Who Achieved a DLQI of 0 or 1 at Weeks 4, 8, and 12 (mITT Analysis Set)

		Zasocitinib			
End Point[a]	**Placebo (n=51)**	**2 mg QD (n=48)**	**5 mg QD (n=51)**	**15 mg QD (n=53)**	**30 mg QD (n=51)**
Week 4					
No. of patients (%)[b]	3 (6)	2 (4)	3 (6)	14 (26)	13 (26)
Proportion difference vs. placebo, % (95% CI)[c]	–	–2 (–10, 7)	0 (–9, 9)	21 (7, 34)	20 (6, 33)
Week 8					
No. of patients (%)[b]	5 (10)	6 (13)	10 (20)	24 (45)	23 (45)
Proportion difference vs. placebo, % (95% CI)[c]	–	3 (–10, 15)	10 (–4, 23)	35 (20, 51)	35 (19, 51)
Week 12					
No. of patients (%)[b]	8 (16)	10 (21)	15 (29)	31 (59)	23 (45)
Proportion difference vs. placebo, % (95% CI)[c]	–	5 (–10, 20)	14 (–2, 30)	43 (26, 59)	29 (13, 46)

Abbreviations: CI, confidence interval; CMH, Cochran–Mantel–Haenszel; DLQI, Dermatology Life Quality Index; MH, Mantel–Haenszel; mITT, modified intent-to-treat; QD, once daily; QoL, quality of life.

[a]The DLQI is a 10-question validated questionnaire structured with each question having four alternative responses: “not at all”, “a little”, “a lot”, or “very much” with corresponding scores of 0, 1, 2, and 3, respectively. The questionnaire also includes a “not relevant” answer scored as “0”. The DLQI is calculated by summing the score of each question, resulting in a maximum of 30 and minimum of 0. The higher the score, the greater the impairment of QoL.[30]

[b]Percentages were based on the number of patients with DLQI ≥2 at baseline in each treatment group. Baseline was defined as the last non-missing assessment before or on the first study treatment dosing date if time was available, and before or on the first study treatment dosing date otherwise.

[c]Proportion differences for achievement of DLQI of 0 or 1 were calculated using the MH method. Patients with assessments collected on the day of or after the start of a prohibited medication that was considered as major protocol deviation were set as non-responders.

eTable 3. Protocol Amendments for Phase 2b Study of Zasocitinib in Patients With Moderate-to-Severe Psoriasis

Protocol Amendment Number [date]	Rationale for Amendments
1 [09/02/2021]	1. To update the list of secondary and exploratory efficacy endpoints. 2. To add optional full-body medical photographs and clarify photography for patients consenting to biopsy collection. 3. To clarify the list of highly effective methods of contraception. 4. To clarify the list of prohibited systemic corticosteroid treatments and those leading to discontinuation from study treatment. 5. To clarify that non-live-attenuated vaccines for COVID-19 were allowed during the study. 6. To add an exclusion criterion for patients enrolled in previous studies with zasocitinib. 7. To add COVID-19 mitigation procedures. 8. To update the grade of cytopenia for mandatory, permanent discontinuation from study treatment from Grade ≥2 to Grade ≥3. 9. To add adverse events of special interest related to known adverse effects of Janus kinase inhibitors. 10. To clarify the sample size determination.
2 [02/04/2022]	1. To clarify the process/timing of eligibility assessment prior to randomization. 2. To update the criteria for temporary or permanent discontinuation of study drug in case of cytopenia Common Terminology Criteria for Adverse Events Grade ≥2. 3. To clarify reporting of adverse events and clinically significant laboratory abnormalities. 4. To update the body mass index range and the laboratory tests allowed for tuberculosis screening. 5. To clarify that intra-articular and intrathecal corticosteroid injections were prohibited. 6. To clarify that non-live-attenuated vaccines for COVID-19 boosters were allowed during the study. 7. To clarify the statistical analysis.

eTable 4. Summary of TEAEs by system organ class and preferred term, all periods (safety analysis set)

System organ class and preferred term, n (%)[a]	Placebo (n=52)	Zasocitinib 2 mg QD (n=50)	Zasocitinib 5 mg QD (n=52)	Zasocitinib 15 mg QD (n=53)	Zasocitinib 30 mg QD (n=52)
Patients with at least one TEAE	23 (44)	31 (62)	28 (54)	28 (53)	31 (60)
Blood and lymphatic system disorders	6 (12)	3 (6)	1 (2)	2 (4)	2 (4)
Neutropenia	3 (6)	2 (4)	0	0	1 (2)
Lymphopenia	3 (6)	0	0	1 (2)	0
Anemia	1 (2)	0	1 (2)	0	1 (2)
Leukopenia	2 (3.8)	1 (2)	0	0	0
Eosinophilia	0	1 (2)	0	1 (2)	0
Monocytosis	0	1 (2)	0	0	0
Thrombocytopenia	0	1 (2)	0	0	0
Cardiac disorders	1 (2)	0	1 (2)	1 (2)	1 (2)
Atrial fibrillation	1 (2)	0	0	0	0
Pericardial effusion	0	0	0	1 (2)	0
Tachycardia	0	0	1 (2)	0	0
Ventricular tachycardia	0	0	0	0	1 (2)
Ear and labyrinth disorders	1 (2)	0	0	1 (2)	0
Ear pain	0	0	0	1 (2)	0
Tympanic membrane perforation	1 (2)	0	0	0	0
Eye disorders	0	0	0	0	1 (2)
Eye irritation	0	0	0	0	1 (2)
Gastrointestinal disorders	2 (4)	4 (8)	3 (6)	6 (11)	6 (12)
Aphthous ulcer	1 (2)	0	1 (2)	2 (4)	2 (4)
Diarrhea	1 (2)	3 (6)	1 (2)	1 (2)	0
Nausea	0	0	1 (2)	0	2 (4)
Abdominal pain	0	1 (2)	0	0	0
Constipation	0	0	0	1 (2)	0
Dental caries	0	0	0	1 (2)	0
Flatulence	0	0	0	0	1 (2)
Gastritis	0	0	0	1 (2)	0
Toothache	0	0	1 (2)	0	0
Vomiting	0	0	0	0	1 (2)
General disorders and administration site conditions	0	0	0	1 (2)	0
Mucosal pain	0	0	0	1 (2)	0

Infections and infestations	7 (13)	12 (24)	10 (19)	12 (23)	14 (27)
COVID-19	1 (2)	6 (12)	4 (8)	6 (11)	7 (13)
Urinary tract infection	1 (2)	2 (4)	2 (4)	1 (2)	2 (4)
Upper respiratory tract infection	1 (2)	2 (4)	0	2 (4)	1 (2)
Gastroenteritis	1 (2)	0	0	2 (4)	0
Oral herpes	0	1 (2)	0	0	2 (4)
Nasopharyngitis	1 (2)	1 (2)	0	0	0
Bronchitis	0	0	1 (2)	0	0
Eczema herpeticum	0	0	0	0	1 (2)
Folliculitis	0	0	0	1 (2)	0
Herpes zoster	0	0	1 (2)	0	0
Influenza	0	0	1 (2)	0	0
Perichondritis	0	1 (2)	0	0	0
Pharyngitis	0	0	0	0	1 (2)
Pneumonia	1 (2)	0	0	0	0
Puncture site infection	0	0	1 (2)	0	0
Sinusitis	0	0	0	1 (2)	0
Suspected COVID-19	0	0	0	0	1 (2)
Tooth infection	1 (2)	0	0	0	0
Injury, poisoning and procedural complications	0	3 (6)	1 (2)	0	3 (6)
Muscle rupture	0	1 (2)	0	0	1 (2)
Corneal abrasion	0	1 (2)	0	0	0
Foot fracture	0	1 (2)	0	0	0
Tendon rupture	0	0	0	0	1 (2)
Thermal burn	0	0	0	0	1 (2)
Tooth fracture	0	0	1 (2)	0	0
Investigations	3 (6)	11 (22)	10 (19)	5 (9)	9 (17)
Blood creatine phosphokinase increased	2 (4)	2 (4)	2 (4)	3 (6)	3 (6)
Lymphocyte count decreased	0	2 (4)	3 (6)	2 (4)	2 (4)
Alanine aminotransferase increased	0	3 (6)	0	0	1 (2)
Blood pressure increased	0	0	2 (4)	0	1 (2)
Neutrophil count decreased	0	2 (4)	0	0	1 (2)
Blood glucose increased	0	1 (2)	1 (2)	0	0
Monocyte count increased	0	1 (2)	1 (2)	0	0
Neutrophil count increased	0	0	1 (2)	0	1 (2)
White blood cell count increased	0	0	1 (2)	0	1 (2)

Aspartate aminotransferase increased	0	1 (2)	0	0	0
Blood calcium decreased	0	1 (2)	0	0	0
Blood cholesterol abnormal	0	0	0	0	1 (2)
Blood sodium decreased	0	0	1 (2)	0	0
Blood triglycerides increased	0	0	0	0	1 (2)
Electrocardiogram abnormal	0	0	0	0	1 (2)
Gamma-glutamyltransferase increased	1 (2)	0	0	0	0
International normalized ratio abnormal	0	0	0	0	1 (2)
International normalized ratio increased	0	0	1 (2)	0	0
Lymphocyte percentage decreased	0	0	1 (2)	0	0
Neutrophil percentage increased	0	0	1 (2)	0	0
Platelet count decreased	0	0	1 (2)	0	0
Platelet count increased	0	0	1 (2)	0	0
Prothrombin time abnormal	0	0	0	0	1 (2)
Prothrombin time prolonged	0	0	1 (2)	0	0
Urine leukocyte esterase positive	0	0	1 (2)	0	0
White blood cell count decreased	0	1 (2)	0	0	0
Metabolism and nutrition disorders	2 (4)	3 (6)	1 (2)	1 (2)	1 (2)
Gout	2 (4)	0	0	0	0
Decreased appetite	0	1 (2)	0	0	0
Diabetes mellitus inadequate control	0	0	0	0	1 (2)
Hypercholesterolemia	0	0	1 (2)	0	0
Hyperglycemia	0	1 (2)	0	0	0
Hypertriglyceridemia	0	0	1 (2)	0	0
Hypoglycemia	0	0	0	1 (2)	0
Hypokalemia	0	1 (2)	0	0	0
Musculoskeletal and connective tissue disorders	3 (6)	2 (4)	2 (4)	1 (2)	5 (10)
Arthralgia	0	1 (2)	2 (4)	0	2 (4)
Back pain	0	0	0	0	2 (4)
Musculoskeletal chest pain	1 (2)	0	0	0	1 (2)
Bursitis	0	0	0	1 (2)	0
Limb discomfort	0	1 (2.0)	0	0	0
Muscle spasms	1 (2)	0	0	0	0
Plantar fasciitis	1 (2)	0	0	0	0

Nervous system disorders	0	1 (2.0)	4 (8)	3 (6)	1 (2)
Headache	0	1 (2.0)	1 (2)	2 (4)	0
Dizziness	0	0	1 (2)	1 (2)	1 (2)
Paresthesia	0	0	1 (2)	0	0
Syncope	0	0	1 (2)	0	0
Psychiatric disorders	0	0	0	0	1 (2)
Panic attack	0	0	0	0	1 (2)
Renal and urinary disorders	1 (2)	1 (2.0)	0	1 (2)	1 (2)
Hematuria	1 (2)	0	0	1 (2)	0
Proteinuria	0	0	0	1 (2)	1 (2)
Leukocyturia	1 (2)	0	0	0	0
Pollakiuria	0	1 (2.0)	0	0	0
Reproductive system and breast disorders	0	0	1 (2)	0	0
Ovarian cyst ruptured	0	0	1 (2)	0	0
Respiratory, thoracic and mediastinal disorders	0	0	1 (2)	1 (2)	2 (4)
Dyspnea	0	0	0	1 (2)	1 (2)
Sinus congestion	0	0	1 (2)	0	1 (2)
Cough	0	0	1 (2)	0	0
Oropharyngeal pain	0	0	0	0	1 (2)
Pleural effusion	0	0	0	1 (2)	0
Skin and subcutaneous tissue disorders	1 (2)	2 (4)	6 (12)	9 (17)	8 (15)
Acne	0	0	1 (2)	3 (6)	2 (4)
Acneiform dermatitis	0	0	1 (2)	1 (2)	3 (6)
Pruritus	0	2 (4)	1 (2)	0	0
Rash	0	0	1 (2)	1 (2)	1 (2)
Rash (maculopapular)	0	0	1 (2)	0	1 (2)
Rosacea	0	0	1 (2)	1 (2)	0
Dermatitis	1 (2)	0	0	0	0
Dermatitis (contact)	0	0	0	1 (2)	0
Intertrigo	0	0	0	1 (2)	0
Miliaria	0	0	0	0	1 (2)
Perioral dermatitis	0	0	0	1 (2)	0
Psoriasis	0	0	1 (2)	0	0
Vascular disorders	0	1 (2)	1 (2)	0	1 (2)
Hypertension	0	1 (2)	1 (2)	0	0
Hypertensive urgency	0	0	0	0	1 (2)

Abbreviations: MedDRA, Medical Dictionary for Regulatory Activities; QD, once daily; TEAE, treatment emergent adverse event.

[a]TEAEs are defined as any adverse events with an onset date on or after the first study treatment dosing and not related to a day 1 pre-dose study assessment, coded using MedDRA version 24.0. Patients experiencing multiple adverse events within the same system organ class are counted only once for that system organ class. Similarly, patients experiencing multiple adverse events within the same preferred term are counted only once within that preferred term.