Supplementary Online Content

Blauvelt A, Leonardi CL, Gooderham M, et al. Efficacy and safety of continuous risankizumab therapy vs treatment withdrawal in patients with moderate to severe plaque psoriasis: a phase 3 randomized clinical trial. *JAMA Dermatol*. Published online April 8, 2020. doi:10.1001/jamadermatol.2020.0723

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

eMethods. Detailed methodology

Outcome assessments

Efficacy outcomes were assessed at every 4 weeks from week 4 to 52, and every 6 weeks from week 58 to 88 as well as during the follow-up period at weeks 94 and 104. Dermatology Life Quality Index (DLQI) outcomes were collected at baseline and weeks 12 and 16. For relapsed patients re-treated with risankizumab, efficacy outcomes were assessed 0, 8, and 16 weeks after the start of re-treatment. In all patients receiving at least one dose of study drug, safety was monitored throughout the trial and for up to 105 days after the last treatment dose.

Psoriasis Area and Severity Index (PASI)

PASI is a validated[1] and widely used clinical efficacy measure in psoriasis that measures the severity of erythema, infiltration, and desquamation weighted by the area of skin involvement over four body regions (head, trunk, upper extremities, and lower extremities).[2] The scores range from 0 (no disease) to 72 (maximal disease activity). The area of psoriatic involvement in the four body regions is given a numerical value (0, no involvement; 1, <10% involvement; 2, 10% to <30% involvement; 3, 30% to <50% involvement; 4, 50% to <70% involvement; 5, 70% to <90% involvement; and 6, 90% to 100% involvement). The severity of erythema, infiltration, and desquamation of lesions are assessed using a numeric scale 0–4 (where 0 is a complete lack of cutaneous involvement and 4 is the severest possible involvement).

In clinical trials, ≥75% improvement in the PASI score (PASI 75) is often considered as clinically meaningful improvement.[2]

Static Physician Global Assessment (sPGA)

The sPGA is a validated efficacy measure[1] based on the physician's assessment of the average thickness, erythema, and scaling of all psoriatic lesions on a 5-point scale with scores ranging from 0 (clear) to 4 (severe).[3] Patients with clear (0) or almost clear (1) are common treatment targets. The assessment is considered "static", which refers to the patient's disease state at the time of the assessments, without comparison to any of the patient's previous disease states.[3]

Dermatology Life Quality Index (DLQI)

The DLQI is a validated[3] patient-administered, 10-question, quality of life questionnaire that covers six domains: symptoms and feelings (questions 1 and 2), daily activities (questions 3 and 4), leisure (questions 5 and 6), work and school (question 7), personal relationships (questions 8 and 9) and treatment (question 10).[4] Responses to each question range from 0 (not relevant/not at all) to 3 (very much), with the exception of question 7, which includes "yes/no" options, where "yes" is scored as 3. The DLQI total score is calculated by summing the scores of each question and ranges from 0 to 30 (the higher the score, the more the quality of life is impaired).[4] If the answer to a question is missing, that domain is treated as missing. If 2 or more questions are left unanswered (missing), DLQI total score is treated as missing. Patients achieving DLQI 0/1 (no effect on patients' life) is a common clinical trial endpoint. A 5-point change from baseline is considered a clinically important difference.

Statistical analyses

A hierarchical testing procedure was conducted for the co-primary (PASI 90 and sPGA 0/1 at week 16, risankizumab vs placebo) and ranked secondary endpoints (PASI 75, PASI 100, sPGA 0, and DLQI 0/1 at week 16 risankizumab vs placebo) in part A1 among in the intention-to-treat (ITT) population defined as all patients randomized at baseline. Independent of the part A1 analysis, a hierarchical testing procedure was conducted for the primary (sPGA 0/1 at week 52, continuous risankizumab vs withdrawal to placebo) and ranked secondary endpoints (sPGA 0/1 at week 104, continuous risankizumab vs withdrawal to placebo) among ITT population in part B, defined as patients who were initially randomized to risankizumab, achieved sPGA 0/1 at week 28 and were re-randomized. In both parts, a step-down procedure was used to test each comparison at a significance level of 0.05 with the overall α level preserved at 0.05. All primary and ranked secondary endpoints were categorical and, as such, were tested using the Cochran-Mantel-Haenszel risk difference estimate stratified by baseline weight (≤100 kg vs >100 kg) and prior exposure to a TNF-α inhibitor (0 vs ≥1). Sensitivity analyses were also performed on the primary and ranked secondary endpoints, among pre-defined per-protocol populations in part A1 and in part B. Missing efficacy data were handled using a non-responder imputation (NRI) method. Analyses were conducted using SAS® version 9.4 (SAS Institute, Inc., Cary, NC) or higher using the UNIX operating system. An independent data monitoring committee, including external safety experts not directly involved in the trial, reviewed unblinded

data during the trial. Clinical site personnel and the study team remained blinded throughout the trial. There were no efficacy analyses for early termination of the trial, thus no α adjustments were necessary.

Time-to-relapse and time to loss of response endpoints

Time to relapse (sPGA ≥3) and time to loss-of-response endpoints were performed in ITT B population among those patients who were initially randomized to risankizumab, achieved sPGA 0/1 response at week 28 and were re-randomized. The time to failure events were calculated as follows: patients were considered as failures if they subsequently lost the response or discontinued from the study due to an adverse event of "worsening of disease under study," or received retreatment with risankizumab. The following equation was used: Time to failure = [date of failure] – [date of first dose in part B] + 1. Patients who maintained the endpoint throughout the study or discontinued from the study due to reasons other than above were censored at their last measurement. Time to relapse and loss of response were analyzed using Kaplan-Meier estimates for each treatment group; treatments were compared using stratified Log-rank test.

eTable 1. Inclusion and exclusion criteria
Inclusion criteria

1. Male or female patients. Women of childbearing potential* must be ready and able to use highly effective methods of birth control per ICH M3(R2) that result in a low failure rate of less than 1% per year when used consistently and correctly. A list of contraception methods meeting these criteria is provided in the patient information.

     *Women of childbearing potential are defined as:
   - Having experienced menarche and are
   - Not postmenopausal (12 months with no menses without an alternative medical cause) and are
   - Not permanently sterilized (e.g., tubal occlusion, hysterectomy, bilateral oophorectomy, or bilateral salpingectomy)
2. Age ≥18 years at screening
3. Have a diagnosis of chronic plaque psoriasis (with or without psoriatic arthritis) at least 6 months before the first administration of study drug. Duration of diagnosis may be reported by the patient.
4. Have stable moderate-to-severe chronic plaque psoriasis with or without psoriatic arthritis at both Screening and Baseline (Randomization);
   - Have an involved body surface area (BSA) ≥10% and
   - Have a Psoriasis Area and Severity Index (PASI) ≥12 and
   - Have a static Physician Global Assessment (sPGA) score of ≥3
5. Must be a candidate for systemic therapy or phototherapy for psoriasis treatment, as assessed by the investigator
6. Signed and dated written informed consent prior to admission to the study and performance of any study procedures in accordance with GCP and local legislation

Exclusion criteria

1. Patients with
   - Non-plaque forms of psoriasis (including guttate, erythrodermic, or pustular)
   - Current drug-induced psoriasis (including a new onset of psoriasis or an exacerbation of psoriasis from beta blockers, calcium channel blockers, or lithium)
   - Active ongoing inflammatory diseases other than psoriasis and psoriatic arthritis that might confound trial evaluations according to the investigator's judgment
2. Previous exposure to BI 655066 (risankizumab)
3. Currently enrolled in another investigational study or less than 30 days (from screening) since completing another investigational study (participation in observational studies is permitted)
4. Use of any restricted medication or any drug considered likely to interfere with the safe conduct of the study
   - Guselkumab or tildrakizumab not allowed prior to or during trial participation
   - Briakinumab, secukinumab, or ustekinumab allowed if last taken over 6 months prior to randomization
   - Brodalumab or ixekizumab allowed if last taken over 4 months prior to randomization
   - Adalimumab, infliximab, or non-biologic investigational products for psoriasis allowed if last taken over 12 weeks prior to randomization
   - Etanercept allowed if last taken over 6 weeks prior to randomization
   - Live virus vaccinations allowed if given over 6 weeks prior to randomization
   - Investigational device or product (excluding psoriasis products) allowed if last used over 30 days prior to randomization
   - Other systemic immunomodulating treatments (e.g. methotrexate, cyclosporine A, corticosteroids, cyclophosphamide, tofacitinib, or apremilast) allowed if last used over 30 days prior to randomization
     - No restriction on corticosteroids with only a topical effect (e.g. inhalant corticosteroids to treat asthma or corticosteroids used in the eye or ear)
   - Other systemic psoriasis treatments (e.g. retinoids, fumarates, or any other drug known to possibly benefit psoriasis) allowed if last used over 30 days prior to randomization
   - Photochemotherapy (e.g., PUVA) allowed if last used over 30 days prior to randomization

- Phototherapy (e.g., UVA, UVB) allowed if last used over 14 days prior to randomization
- Topical treatment for psoriasis or any other skin condition (e.g., corticosteroids, vitamin D analogues, vitamin A analogues, pimecrolimus, retinoids, salicylvaseline, salicylic acid, lactic acid, tacrolimus, tar, urea, andanthralin, α-hydroxy, fruit acids) allowed if last used over 14 days prior to randomization
  - *Exception*: Topical steroids of US class 6 (mild, such as Desonide) or US class 7 (least potent, such as hydrocortisone) were permitted for use limited to the face, axilla, and/or genitalia with a restriction of use within 24 hours prior to clinic visits when PASI is assessed

5. Major surgery performed within 12 weeks prior to randomization or planned within 12 months after screening (e.g., hip replacement, removal aneurysm, stomach ligation)
6. Known chronic or relevant acute infections, such as HIV, viral hepatitis, or tuberculosis. QuantiFERON® TB test or PPD skin test will be performed during screening. Patients with a positive test result may participate in the study if further work up (according to local practice/guidelines) establishes conclusively that the patient has no evidence of active tuberculosis. If presence of latent tuberculosis is established, patients who are at low risk of reactivation, defined by local guidelines and investigator judgment, do not need to be treated with prophylactic anti-tuberculosis prior to or during the trial.
7. Any documented active or suspected malignancy or history of malignancy within 5 years prior to screening, except appropriately treated basal cell carcinoma or squamous cell carcinoma of the skin or in situ carcinoma of uterine cervix
8. Evidence of a current or previous disease (including chronic alcohol or drug abuse), medical condition other than psoriasis, surgical procedure (i.e., organ transplant), medical examination finding (including vital signs and ECG), or laboratory value at the screening visit outside the reference range that in the opinion of the Investigator, is clinically significant and would make the study participant unable to adhere to the protocol or to complete the trial, compromise the safety of the patient, or compromise the quality of the data
9. History of allergy/hypersensitivity to a systemically administered biologic agent or its excipients
10. Women who are pregnant, nursing, or who plan to become pregnant while in the trial
11. Previous enrolment in this trial

eTable 2. List of ranked secondary endpoints in parts A and B

Part A	
Rank	**Secondary Endpoints**
1st	PASI 75 at week 16 vs Placebo
2nd	PASI 100 response at week 16 vs Placebo
3rd	sPGA 0 (clear) response at week 16 vs Placebo
4th	DLQI score of 0 or 1 response at week 16 vs Placebo
Part B	
Rank	**Secondary Endpoint**
1st	sPGA 0 or 1 (clear or almost clear) response at week 104 vs. switching to placebo
Multiplicity was controlled using a hierarchical testing (statistically significant results for the comparison in the higher rank [primary followed by ranked secondary endpoints] were necessary to initiate testing of the next comparison in the lower rank) for the ranked secondary endpoints. DLQI=Dermatology Life Quality Index. PASI=Psoriasis Area and Severity Index. sPGA=static Physician's Global Assessment.	

eTable 3. Criteria for exclusion of patients from per-protocol populations in parts A1 and B

Part A1*	
Criteria	
1	Patients received no dose of study drug in part A1
2	Patients received <75% of planned study drug injections prior to Week 16
3	Patients have neither a PASI nor sPGA assessment post-baseline during part A1
4	Baseline BSA <10%
5	Baseline PASI <12
6	Baseline sPGA <3
7	Patient took prohibited medication that could potentially affect the assessment of primary and ranked endpoints in part A1
Part B†	
Criteria	
8	Patients received no dose of study drug in part B prior to Week 52
9	Patients received <75% of planned study drug injections in part B prior to Week 52
10	Patients had no sPGA assessment post re-randomization during part B
11	Patients had sPGA >1 at re-randomization
12	Patient took prohibited medication that could potentially affect the assessment of ranked endpoints in part B

*Patients meeting any of the listed criteria 1–7 were excluded from the Per-Protocol analyses in part A1.
†Patients who met any of the criteria 4–7 criteria or any of the criteria 8-12 were excluded from the Per-Protocol population in part B for re-randomized patients.
BSA=body surface area. PASI=Psoriasis Area and Severity Index. sPGA=static Physician's Global Assessment.

eTable 4. Summary of significant protocol deviations (ITT population)*

	Risankizumab (N=407)	Placebo (N=100)
Any protocol deviation	43 (10.6)	6 (6.0)
Inclusion/exclusion criteria deviations	33 (8.1)	4 (4.0)
Received wrong treatment or incorrect dose	5 (1.2)	0
Received excluded or prohibited concomitant treatment	6 (1.5)	2 (2.0)
Developed withdrawal criteria but was not withdrawn	0	0

*Patients with multiple protocol deviations were counted once in each deviation category.
ITT=intention-to-treat.

eTable 5. Baseline demographics and disease characteristics of risankizumab-treated patients re-randomized in Part B (ITT)

Characteristic	RZB re-randomized in Part B N=336
Age, years	50 (38–59)
Sex	
Male	239 (71%)
Female	97 (27%)
Race	
White	259 (77%)
Black or African American	16 (5%)
Asian	57 (17%)
Other	4 (1%)
Weight, kg	87.9 (75.2–102.1)
Weight	
≤100 kg [*]	238 (71%)
>100 kg [*]	98 (29%)
BMI, kg/m^2	29.8 (25.9–34.7)
PASI	17.3 (14.4–21.9)
sPGA	
Moderate	271 (81%)
Severe	65 (19%)
BSA involvement, %	20% (14–31)
Prior non-biologic systemic therapy	160 (48%)
Any prior biologic therapy	182 (54%)
Prior TNFi exposure [*]	112 (33%)
Prior IL-17i exposure [†]	86 (26%)
Prior IL-12/23i exposure [‡]	66 (20%)

Data are n (%) or median (IQR). *Stratification factors at randomization. †Including brodalumab, ixekizumab, and secukinumab. ‡Including ustekinumab and briakinumab. BMI= Body Mass Index. BSA=Body Surface Area. IL-17i=interleukin-17 inhibitor. IL-12/23i=interleukin-12/23 inhibitor. IQR=Interquartile Range. ITT=intention-to-treat. PASI=Psoriasis Area and Severity Index. RZB=Risankizumab. sPGA=static Physician's Global Assessment. TNFi=Tumor Necrosis Factor-α inhibitor.

eTable 6. Co-primary endpoints in part A1 (per protocol)

Part A1	Risankizumab (n=400)	Placebo (n=99)	Risk Difference from Placebo (95% CI)
PASI 90 at week 16	296 (74.0)	2 (2.0)	71.6 (66.4, 76.8)*
sPGA 0/1 at week 16	335 (83.8)	6 (6.1)	77.6 (71.7, 83.5)*
Categorical variables were analyzed using Cochran-Mantel-Haenszel (CMH) risk difference estimates stratified by baseline weight and prior exposure to a tumor necrosis factor inhibitor. Missing data were imputed as non-responders. *P<0.0001 compared with placebo. CI=Confidence Interval. PASI=Psoriasis Area and Severity.			

eTable 7. Primary endpoint in part B (per protocol)

Part B	RZB/RZB (n=109)	RZB/PBO (n=221)	Risk Difference from RZB/PBO (95% CI)
sPGA 0/1 at week 52	96 (88.1)	136 (61.5)	26.4 (17.7, 35.0)*

Categorical variables were analyzed using Cochran-Mantel-Haenszel (CMH) risk difference estimates stratified by baseline weight and prior exposure to a TNF inhibitor. Missing data were imputed as non-responders. *P<0.0001 compared with RZB/PBO. RZB/RZB=continuous risankizumab. RZB/PBO=treatment withdrawal to placebo. CI=Confidence Interval. PASI=Psoriasis Area and Severity.

eTable 8. Common treatment-emergent adverse events reported by ≥5% in any treatment group through parts A and B

Part A	RZB (n=407)	PBO (n=100)
Nasopharyngitis	21 (5.2%)	6 (6.0%)
Upper respiratory tract infection	6 (1.5%)	5 (5.0%)
Psoriasis	2 (0·5%)	5 (5.0%)
Part B	RZB/RZB (n=111)	RZB/PBO (n=225)
Nasopharyngitis	24 (21.6%)	45 (20.0%)
Upper respiratory tract infection	16 (14.4%)	23 (10.2%)
Arthralgia	10 (9.0%)	13 (5.8%)
Headache	8 (7.2%)	7 (3.1%)
Influenza	7 (6.3%)	8 (3.6%)
Back pain	4 (3.6%)	12 (5.3%)
PBO=placebo. RZB=risankizumab. RZB/PBO=re-randomized to placebo. RZB/RZB=re-randomized to risankizumab.		

eTable 9. Overview of treatment-emergent adverse events of interest during parts A1 and B

Part A1	RZB (n=407)	PBO (n=100)
Serious Infections	1 (0.2%)	1 (1.0%)
Abscess on neck	1 (0.2%)	0
Cellulitis	0	1 (1.0%)
Opportunistic infections	0	0
Malignancies	3 (0.7%)	0
Esophageal carcinoma	1 (0.2%)	0
Malignant melanoma in situ	1 (0.2%)	0
Squamous cell carcinoma in situ	1 (0.2%)	0
Hepatic events	3 (0.7%)	2 (2.0%)
Hepatic enzyme increased	1 (0.2%)	0
Hepatic steatosis	2 (0.5%)	1 (1.0%)
Liver injury	0	1 (1.0%)
Part B	**RZB/RZB (n=111)**	**RZB/PBO (n=225)**
Serious Infections	2 (1.8%)	2 (0.9%)
Abdominal abscess	0	1 (0.4%)
Bacterial meningitis	1 (0.9%)	0
Diverticulitis	0	1 (0.4%)
Nasopharyngitis	1 (0.9%)*	0
Periorbital cellulitis	0	1 (0.4%)
Opportunistic infections	1 (0.9%)	1 (0.4%)
Oral candidiasis	1 (0.9%)	1 (0.4%)
Malignancies	2 (1.8%)	6 (2.7%)
B-cell lymphoma	0	1 (0.4%)
Basal cell carcinoma	0	1 (0.4%)
Breast cancer	1 (0.9%)	0
Breast cancer stage 1	0	1 (0.4%)
Metastases to lymph nodes	1 (0.9%)	0
Prostate cancer	1 (0.9%)	2 (0.9%)
Squamous cell carcinoma in situ	0	1 (0.4%)
Hepatic events	8 (7.2%)	5 (2.2%)
ALT increased	2 (1.8%)	1 (0.4%)
AST increased	2 (1.8%)	2 (0.9%)
GGT increased	1 (0.9%)	2 (0.9%)
Hepatic cirrhosis	1 (0.9%)	0
Hepatic steatosis	1 (0.9%)	2 (0.9%)
Hepatitis	1 (0.9%)	0
INR increased	1 (0.9%)	0
Transaminases increased	1 (0.9%)	0

*On Day 224, patient experienced nasopharyngitis and was hospitalized for 2 days; AE was deemed not related to study drug. The course of treatment suggested an underlying allergy. ALT=alanine aminotransferase. AST=aspartate aminotransferase. GGT=gamma-glutamyltransferase. INR=international normalized ratio. PBO=placebo. RZB=risankizumab. RZB/PBO=re-randomized to placebo. RZB/RZB=re-randomized to risankizumab.

eTable 10. Overview of treatment-emergent adverse events in parts A2 and B

| TEAEs, n (%)	Weeks 16 – 28 RZB/RZB (n=400)	Weeks 16 – 104 PBO/RZB (n=93)	Weeks 28 – 104 RZB/RZB/RZB (n=63)
Any adverse event	173 (43.3)	91 (91.4)	53 (84.1)
Serious adverse events	10 (2.5)	11 (11.8)	8 (12.7)
Severe adverse events	7 (1.8)	9 (9.7)	8 (12.7)
Adverse events leading to drug discontinuation	1 (0.3)	3 (3.2)	2 (3.2)
Infections	84 (21.0)	58 (62.4)	34 (54.0)
Serious infections	2 (0·5)	2 (2.2)	1 (1.6)
Active tuberculosis*	0	0	0
Latent tuberculosis	0	0	0
Adjudicated major adverse cardiovascular event	1 (0.3)	2 (2.2)	0
Malignancies	3 (0.8)	2 (2.2)	2 (3.2)
Malignancies excluding non-melanoma skin cancer	0	1 (1.1)	2 (3.2)
Serious hypersensitivity	0	0	0
Deaths (including non-treatment emergent)	0	2 (2.2)	0
*Tuberculosis testing was performed at screening and at the end of treatment using QuantiFERON or PPD skin test. TEAEs=Treatment-Emergent adverse events.			

eTable 11. Overview of treatment-emergent adverse events during re-treatment

TEAEs, n (%)	RZB/PBO/RZB (n=153)	RZB/RZB/RZB (n=4)
Any adverse event	83 (45.7)	2 (50.0)
Serious adverse events	7 (4.6)	0
Severe adverse events	7 (4.6)	0
Adverse events leading to drug discontinuation	0	0
Infections	44 (28.8)	0
Serious infections	1 (0.7)	0
Active tuberculosis*	0	0
Latent tuberculosis	0	0
Adjudicated major adverse cardiovascular event	0	0
Malignancies	1 (0.7)	0
Malignancies excluding non-melanoma skin cancer	1 (0.7)	0
Serious hypersensitivity	0	0
Deaths (including non-treatment emergent)	0	0
*Tuberculosis testing was performed at screening and at the end of treatment using QuantiFERON or PPD skin test. TEAEs=Treatment-Emergent adverse events.		

eTable 12. Treatment-emergent adverse events for all patients treated with risankizumab over 2 years

TEAEs	Patients, n (%) All RZB treated (n=500)	Events, E/100 PYS All RZB treated (n=500; PYS=690.1)
Any adverse event	426 (85.2%)	1792 (259.7)
Serious adverse events	55 (11.0%)	93 (13.5)
Severe adverse events	44 (8.8%)	75 (10.9)
Adverse events leading to drug discontinuation	12 (2.4%)	14 (2.0)
Infections	280 (56.0%)	579 (83.9)
Serious infections	9 (1.8%)	10 (1.4)
Active tuberculosis*	0	0
Latent tuberculosis	0	0
Adjudicated major adverse cardiovascular event	4 (0.8%)	6 (0.9)
Malignancies	13 (2.6%)	15[†] (2.2)
Malignancies excluding non-melanoma skin cancer	8 (1.6%)	10 (1.4)
Hepatic events	23 (4.6%)	37[‡] (5.4)
Serious hypersensitivity	0	0
Deaths (including non-treatment emergent)	4 (0.8%)	4 (0.6)

*Tuberculosis testing was performed at screening and at the end of treatment using QuantiFERON or PPD skin test.

[†]3 events of basal cell carcinoma, 2 events of prostate cancer, 2 events of squamous cell carcinoma of the skin, and 1 event each of breast cancer, gastric cancer, hepatic cancer metastatic, intestinal adenocarcinoma, invasive ductal breast carcinoma, malignant melanoma in situ, metastases to lymph node, and esophageal carcinoma.

[‡]8 events of alanine aminotransferase increased, 7 events of γ-glutamyl transferase increased, 5 events of aspartate aminotransferase increased, 5 events of hepatic steatosis, 3 events of hepatic enzyme increased, 3 events of hepatitis, and 1 event each of blood bilirubin increased, hepatic cirrhosis, hepatosplenomegaly, hypertransaminasemia, international normalized ratio increased, and transaminases increased.

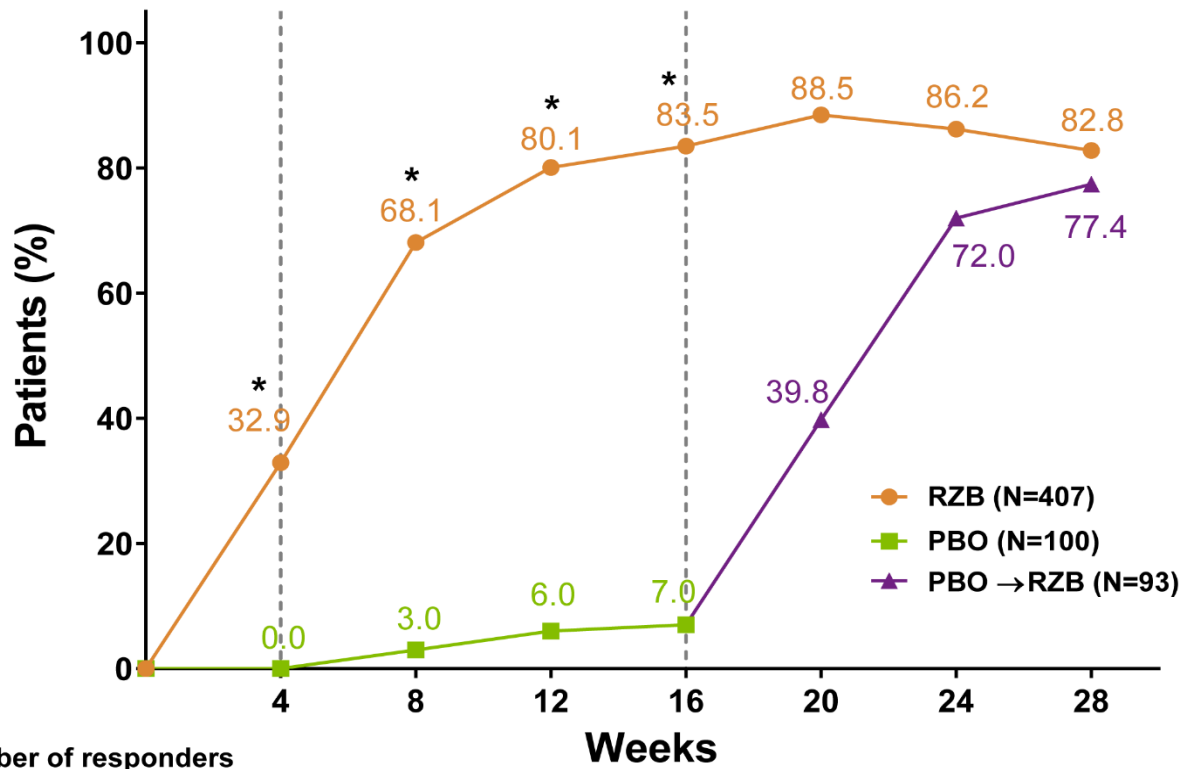TEAEs=Treatment-Emergent adverse events; RZB=risankizumab; PYS=patient years.
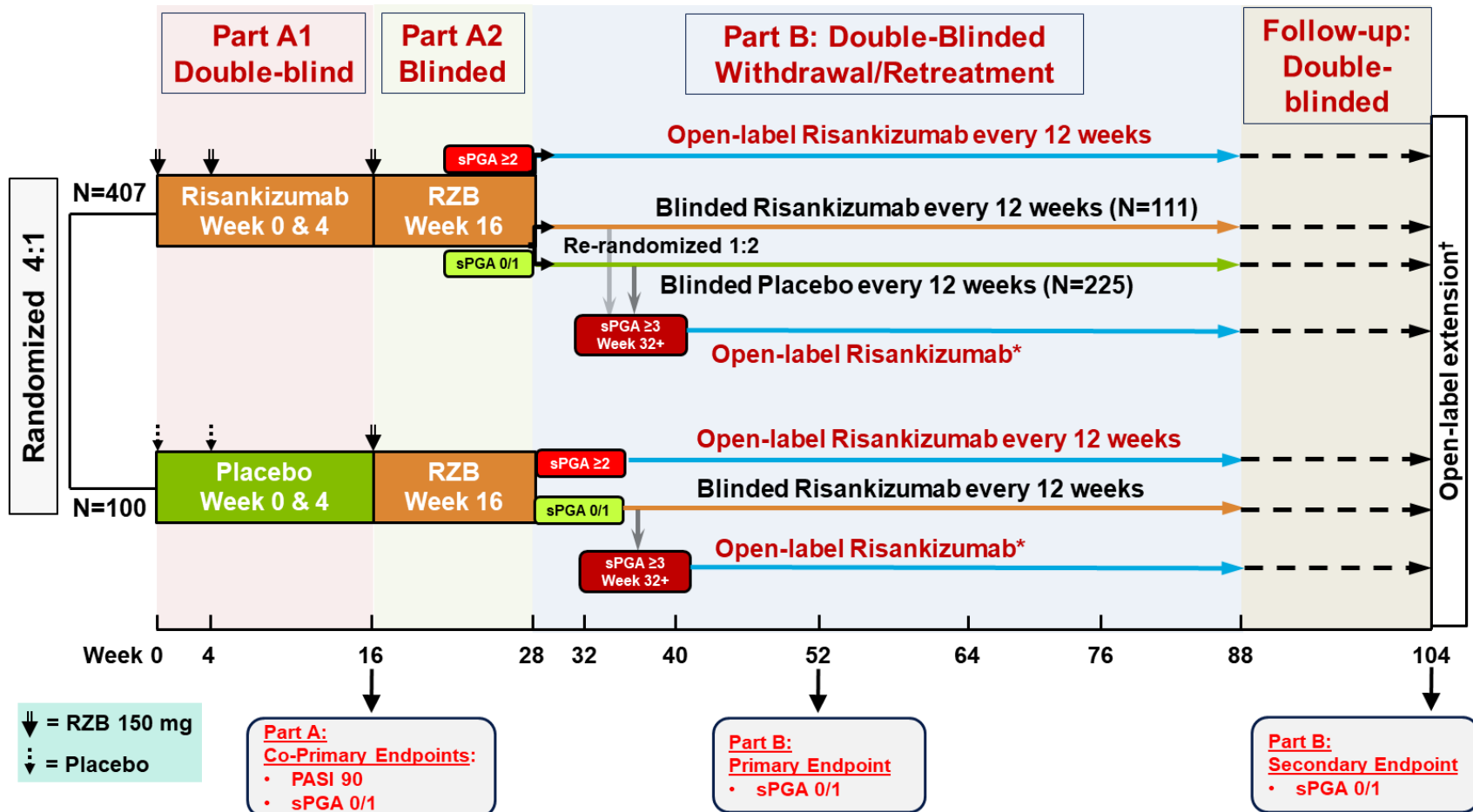
eFigure 1. Study design

*If relapse occurred between week 32 and week 70, open-label risankizumab 150 mg was administered at 0, 4, and 16 weeks (EOT) after relapse. If relapse occurred after week 70 through week 82, open-label risankizumab 150 mg was administered at 0, and 4 weeks (EOT) after relapse. If relapse occurred after week 82 through week 88, the patients were immediately entered into EOT protocol, including the final dose of study drug. †Study completers had the option to enter the open-label extension.
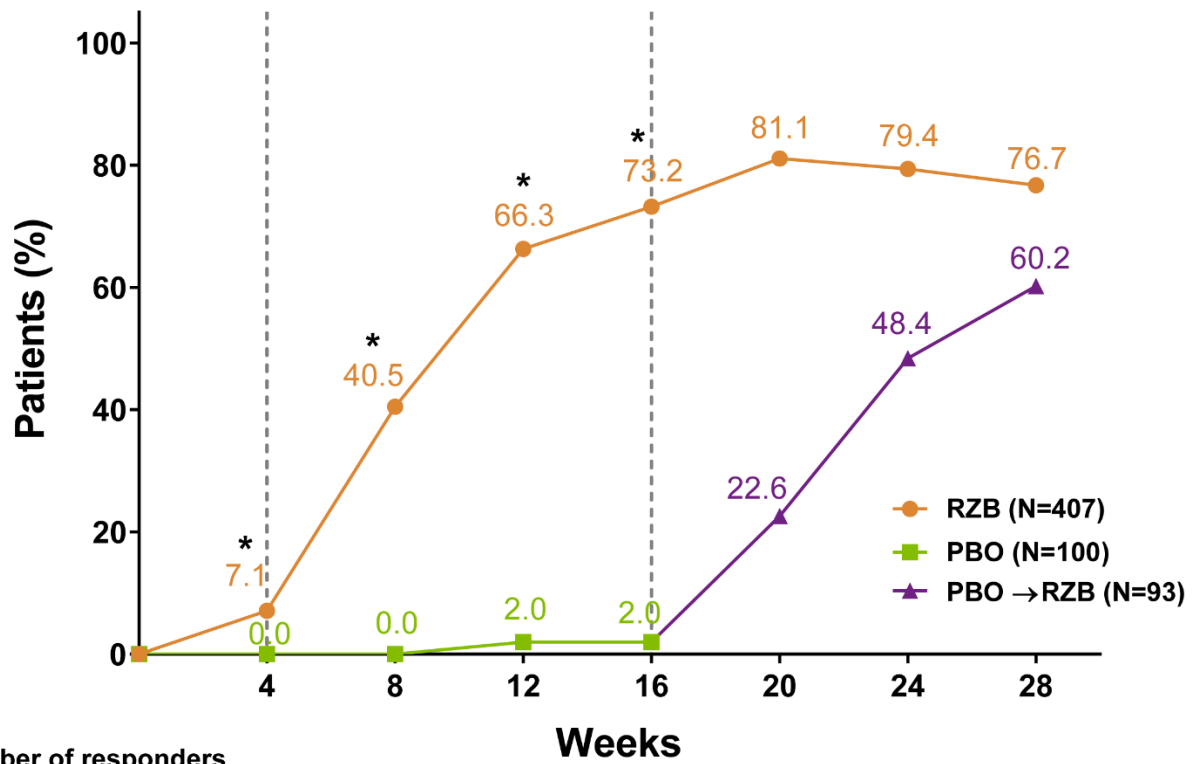
EOT=end of treatment. PASI=Psoriasis Area Severity Index. RZB=risankizumab. sPGA=static Physician's Global Assessment.

eFigure 2. Proportion of patients (non-responder imputation) achieving sPGA 0/1(A), PASI 90 (B), sPGA 0 (C), PASI 100 (D), and DLQI 0/1 (E) responses through part A. Dotted lines indicate risankizumab doses at weeks 4 and 16; an initial dose was given at week 0. The percentage at each datapoint indicates the proportion of patients who achieved the endpoint at each timepoint. *P<.0001 versus placebo based on nominal P value except at week 16. †P=.0463 versus placebo. ‡P=0.0017 versus placebo. DLQI=Dermatology Quality of Life Index. PASI=Psoriasis Area and Severity Index. sPGA= static Physician's Global Assessment.
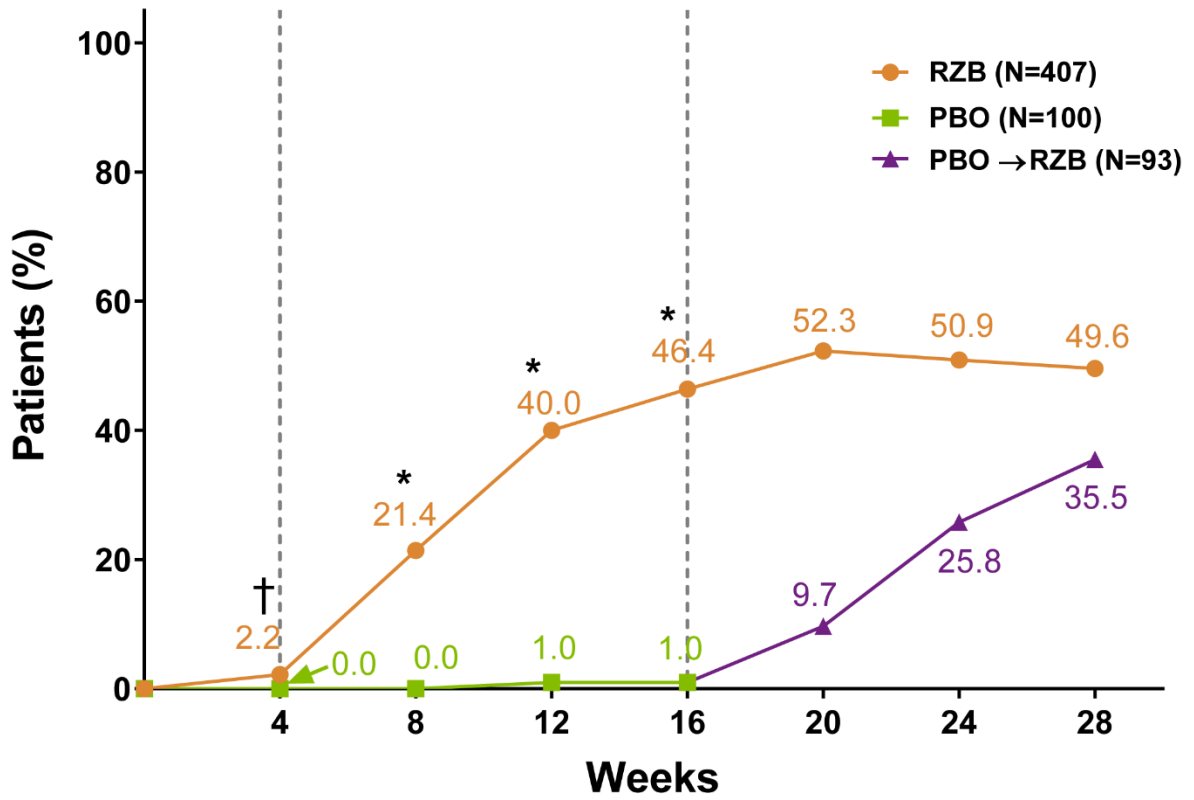
A sPGA 0/1

- RZB (N=407)
- PBO (N=100)
- PBO →RZB (N=93)

Number of responders								
RZB	0	134	277	326	340	360	351	337
PBO/RZB	0	0	3	6	7	37	67	72

B

PASI 90

Chart showing PASI 90 response over weeks. Y-axis: Patients (%), X-axis: Weeks.

- RZB (N=407): 7.1 (wk 4), 40.5 (wk 8), 66.3 (wk 12), 73.2 (wk 16), 81.1 (wk 20), 79.4 (wk 24), 76.7 (wk 28)
- PBO (N=100): 0.0 (wk 4), 0.0 (wk 8), 2.0 (wk 12), 2.0 (wk 16)
- PBO→RZB (N=93): 22.6 (wk 20), 48.4 (wk 24), 60.2 (wk 28)

Legend:
- RZB (N=407)
- PBO (N=100)
- PBO →RZB (N=93)

Number of responders

RZB	0	29	165	270	298	330	323	312
PBO/RZB	0	0	0	2	2	21	45	56

C sPGA 0

Legend:
- RZB (N=407)
- PBO (N=100)
- PBO →RZB (N=93)

RZB values: 2.2, 21.4, 40.0, 46.4, 52.3, 50.9, 49.6
PBO values: 0.0, 0.0, 1.0, 1.0
PBO →RZB values: 9.7, 25.8, 35.5

Y-axis: Patients (%), X-axis: Weeks (4, 8, 12, 16, 20, 24, 28)

Number of responders

RZB	0	9	87	163	189	213	207	202
PBO/RZB	0	0	0	1	1	9	24	33

D

PASI 100

Legend:
- RZB (N=407)
- PBO (N=100)
- PBO →RZB (N=93)

RZB values: 2.2, 21.4, 39.8, 47.2, 52.6, 50.9, 49.6
PBO values: 0.0, 0.0, 1.0, 1.0
PBO→RZB values: 9.7, 25.8, 35.5

X-axis: Weeks — 4, 8, 12, 16, 20, 24, 28
Y-axis: Patients (%) — 0, 20, 40, 60, 80, 100
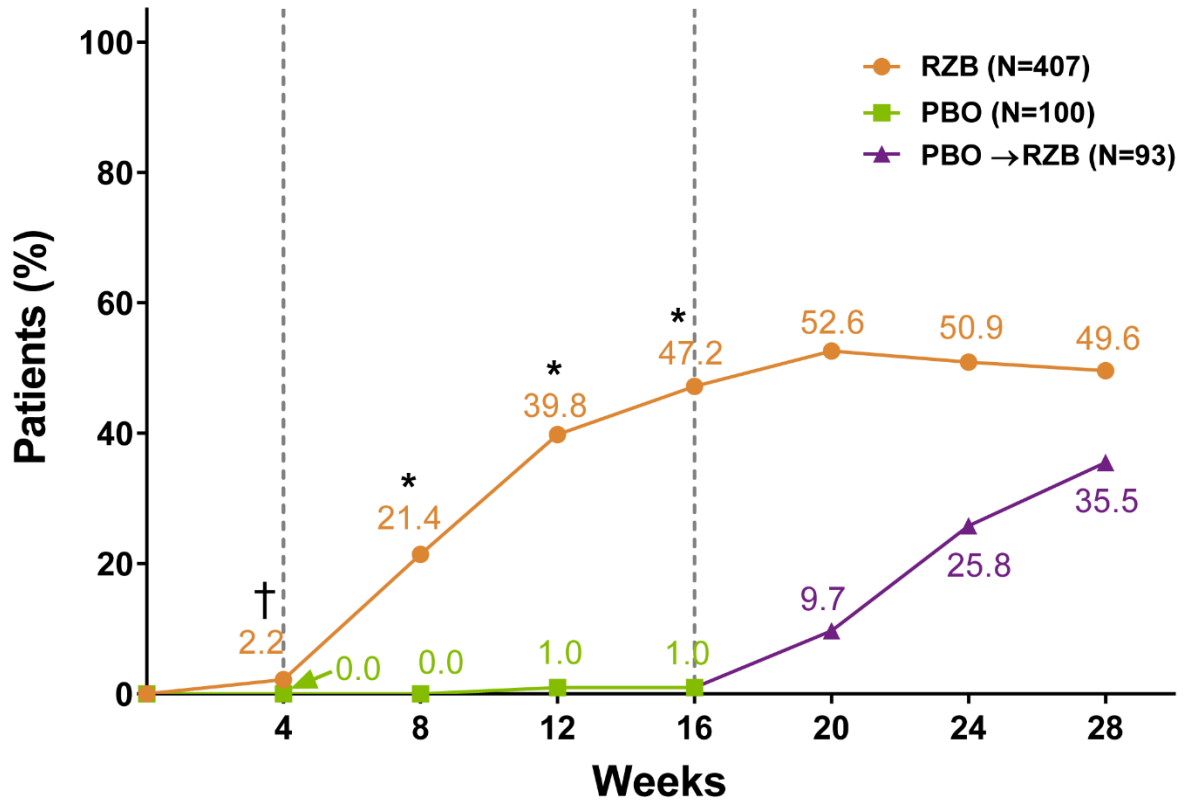
Number of responders

RZB	0	9	87	162	192	214	207	202
PBO/RZB	0	0	0	1	1	9	24	33

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DLQI 0/1

E

Patients (%)

- RZB (N=407)
- PBO (N=100)

2.5

2.0

59.7 *

65.4 *

2.0

3.0

Weeks
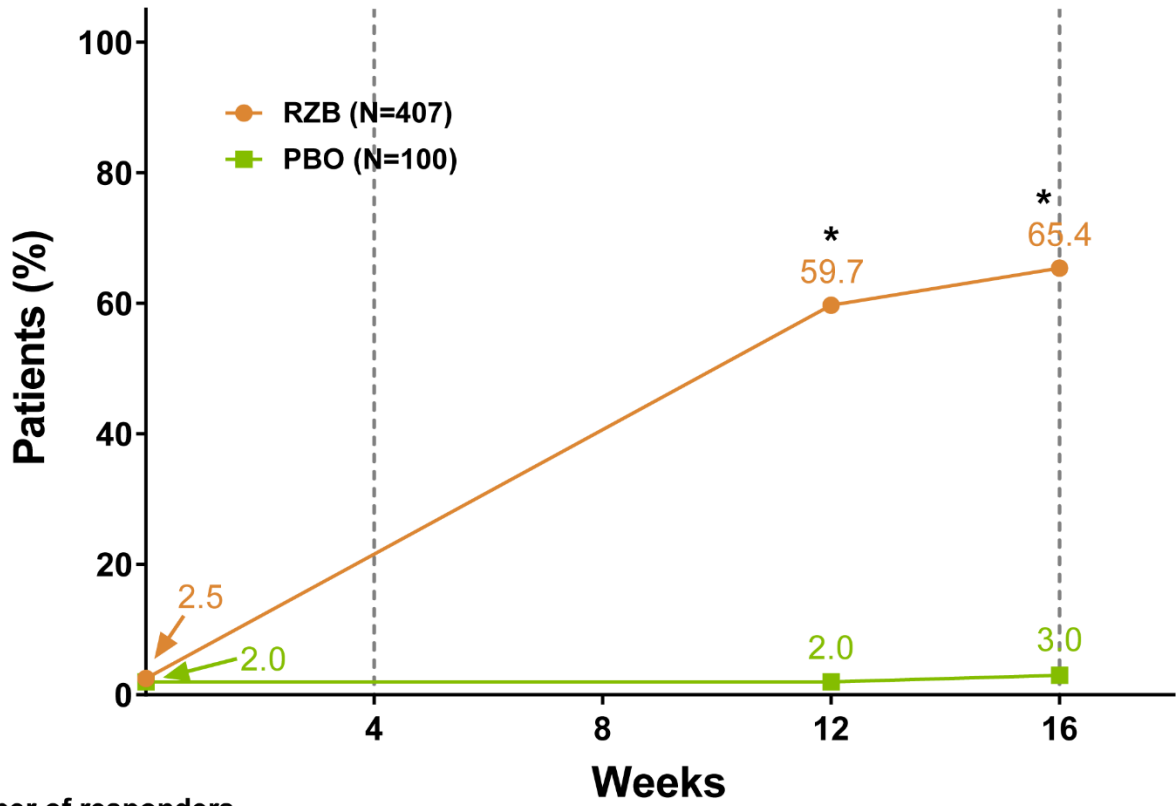
Number of responders

RZB	10	243	266
PBO	2	2	3
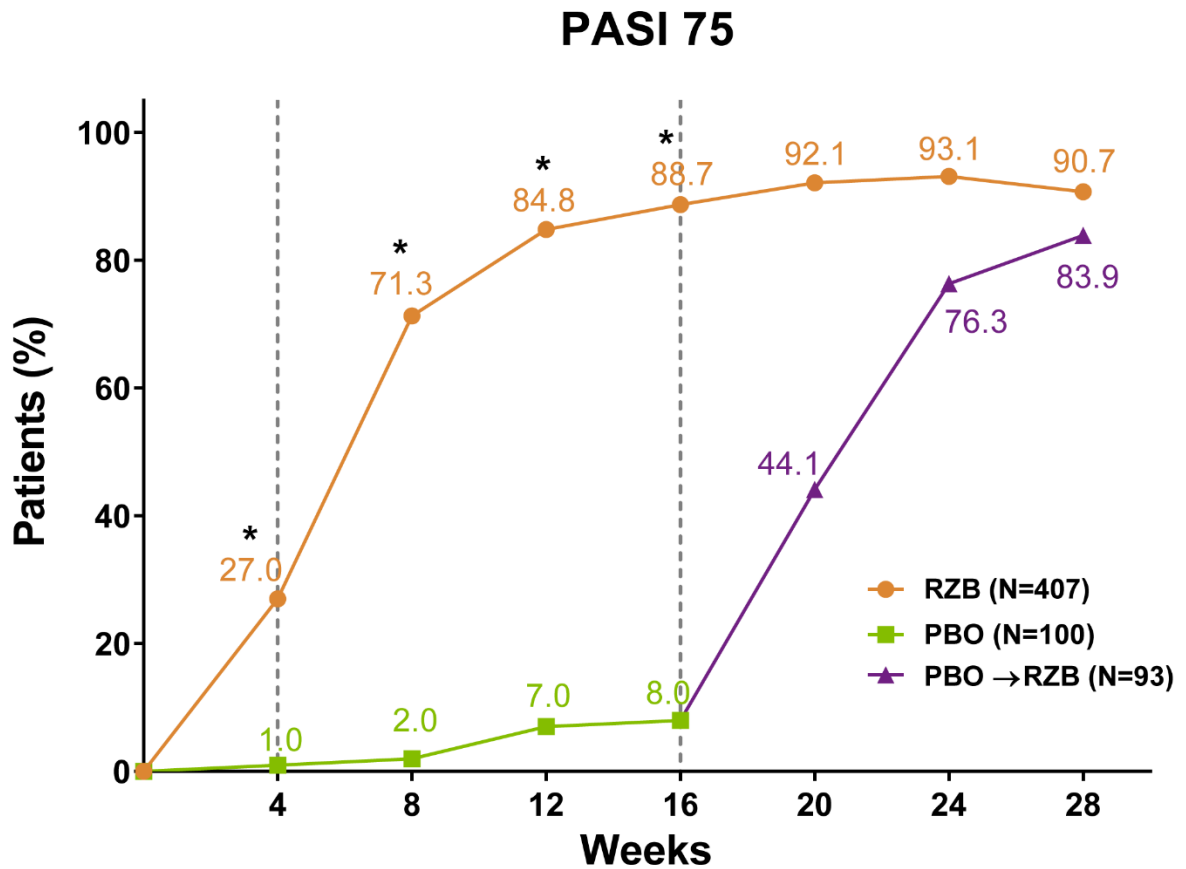
PASI 75

Number of responders

RZB	0	110	290	345	361	375	379	369
PBO/RZB	0	1	2	7	8	41	71	78

eFigure 3. Proportions of patients (non-responder imputation) achieving PASI 75 through part A.

Arrows indicate timepoints where patients received either risankizumab 150 mg or matching placebo. *$P<.0001$ versus placebo based on nominal P value except at week 16. PASI=Psoriasis Area and Severity Index.
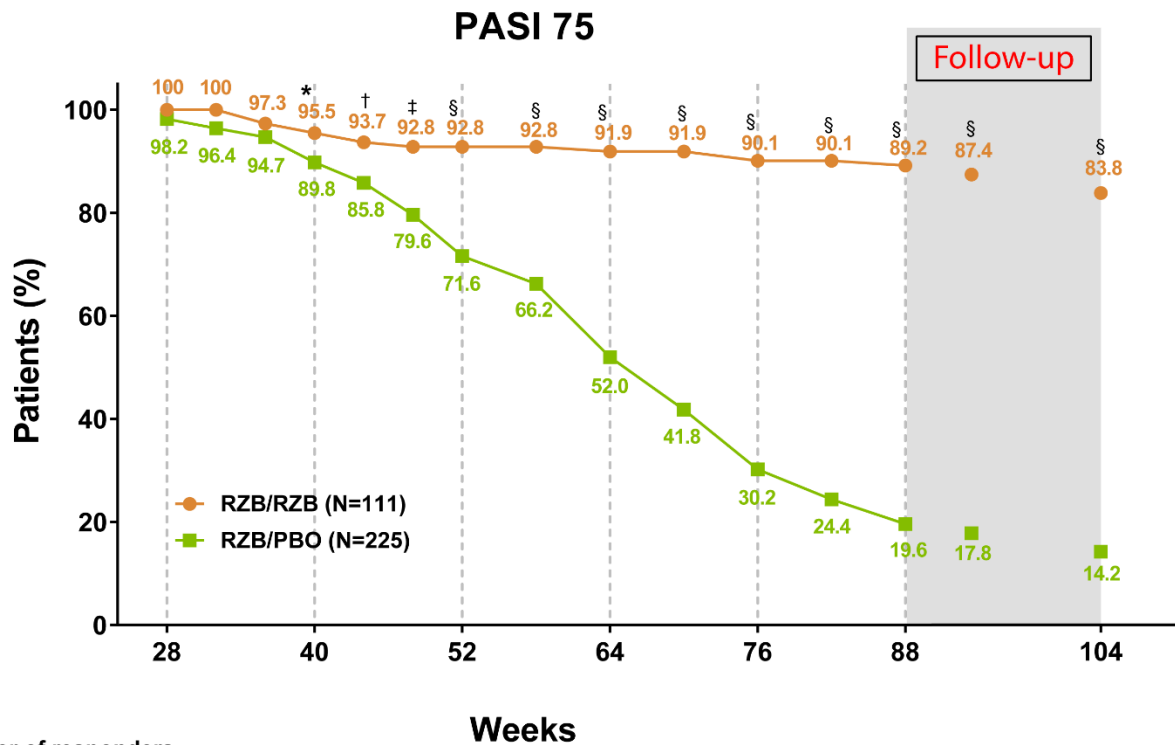
PASI 75

eFigure 4. Proportion of re-randomized patients (non-responder imputation) achieving PASI 75 through part B and follow-up (weeks 28 to 104).

Dotted lines indicate timepoints where patients received either risankizumab 150 mg or matching placebo. *P=.0464 versus placebo based on nominal P value. †P=.0147 versus placebo based on nominal P value. ‡P=.0002 versus placebo based on nominal P value. §P<.001 versus placebo based on nominal P value. PASI=Psoriasis Area and Severity Index.

sPGA 0/1
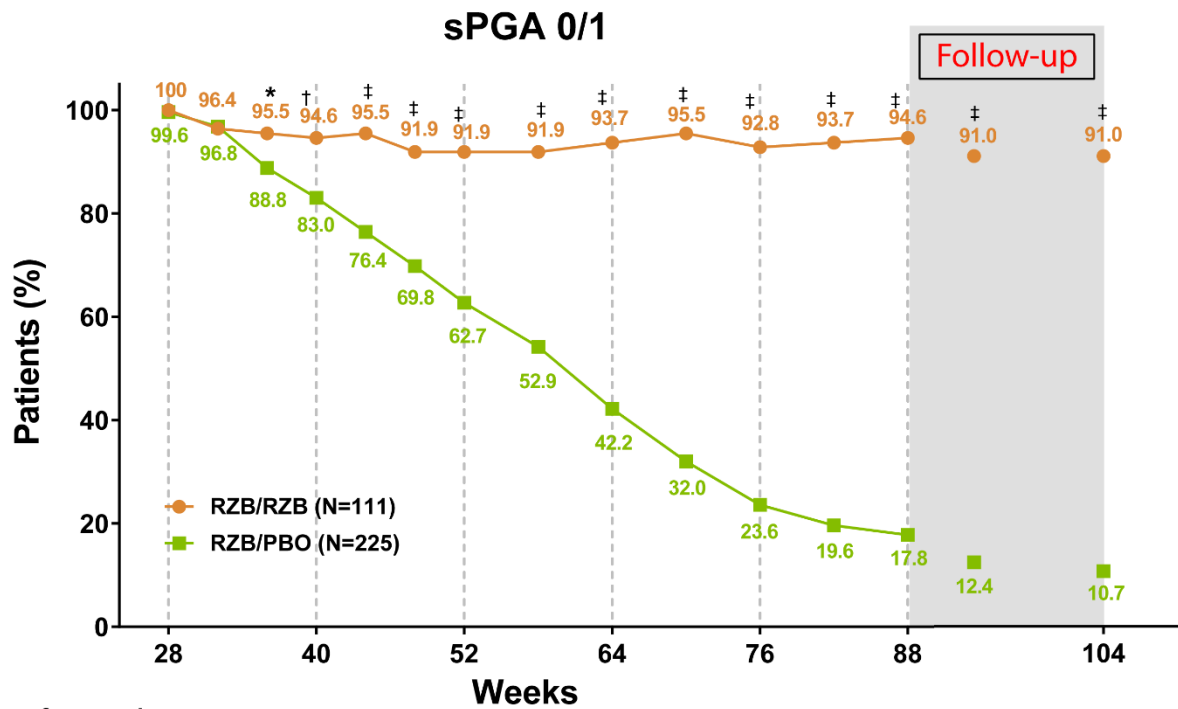
Number of responders	28			40			52		64		76		88		104
RZB/RZB	111	107	106	105	106	102	102	102	104	106	103	104	105	101		101
RZB/PBO	224	214	198	186	172	157	141	122	95	72	53	44	40	28		24

eFigure 5. Proportion of re-randomized patients (last observation carried forward) achieving sPGA 0 or 1 through part B and follow-up (weeks 28 to 104).

Dotted lines indicate timepoints where patients received either risankizumab 150 mg or matching placebo. *P=.0221 versus placebo based on nominal *P* value. †P=.0004 versus placebo based on nominal *P* value except at week 52 and 104. ‡P<.001 versus placebo based on nominal *P* value. sPGA=static Physician's Global Assessment.
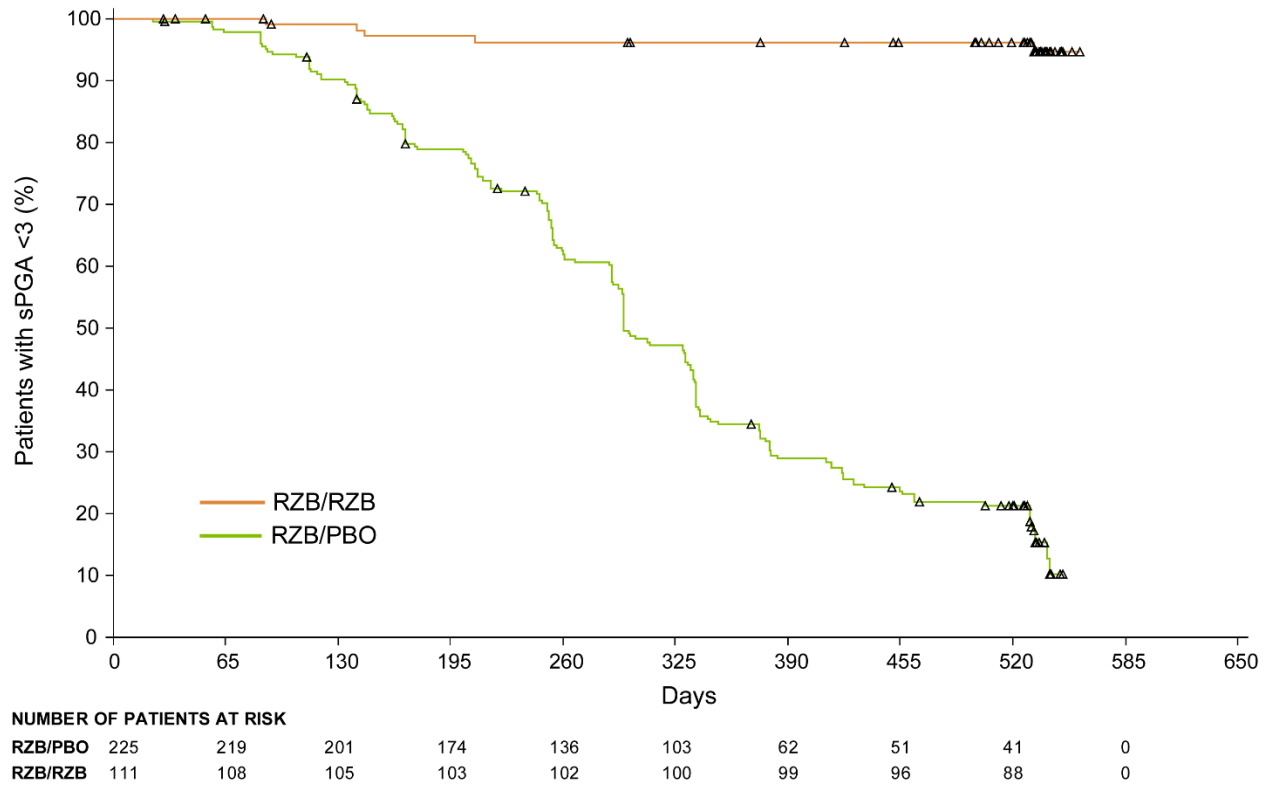
eFigure 6. Time to sPGA ≥3 after re-randomized to either continuous risankizumab or treatment withdrawal to placebo. Triangles represent patients that were censored since they have no data beyond the indicated time point. RZB=risankizumab. PBO=placebo. sPGA=static Physician's Global Assessment.
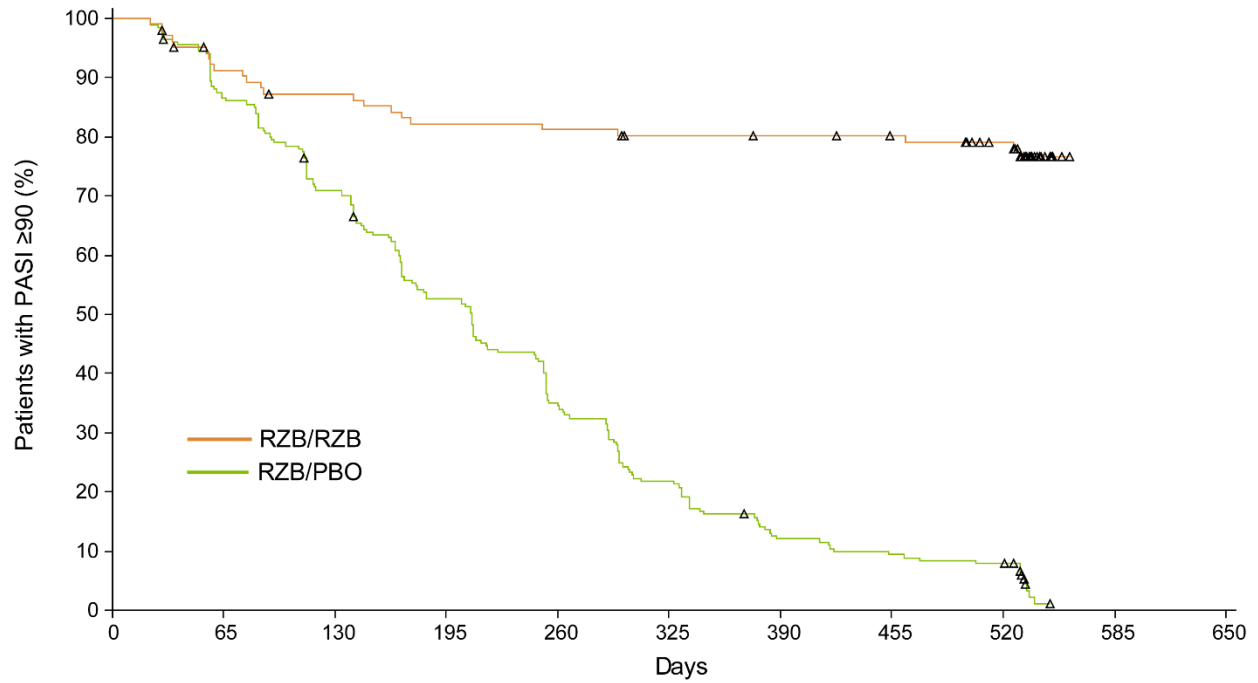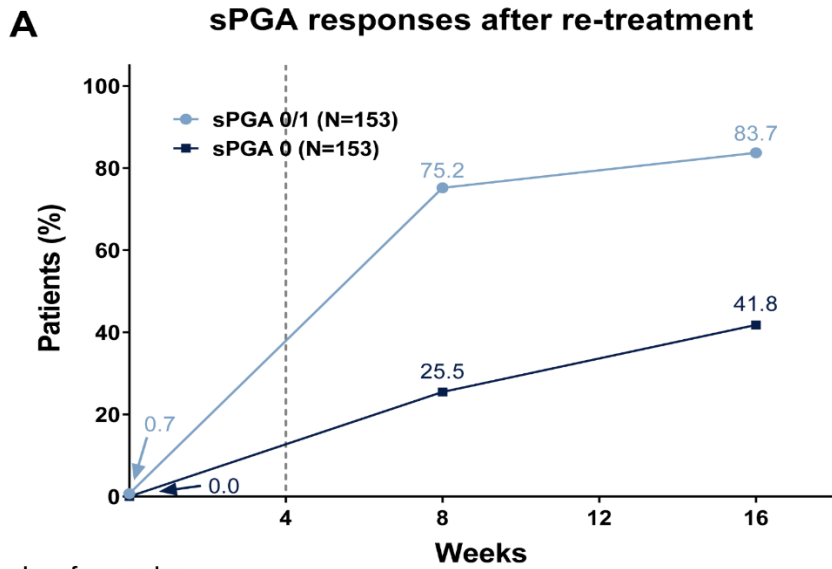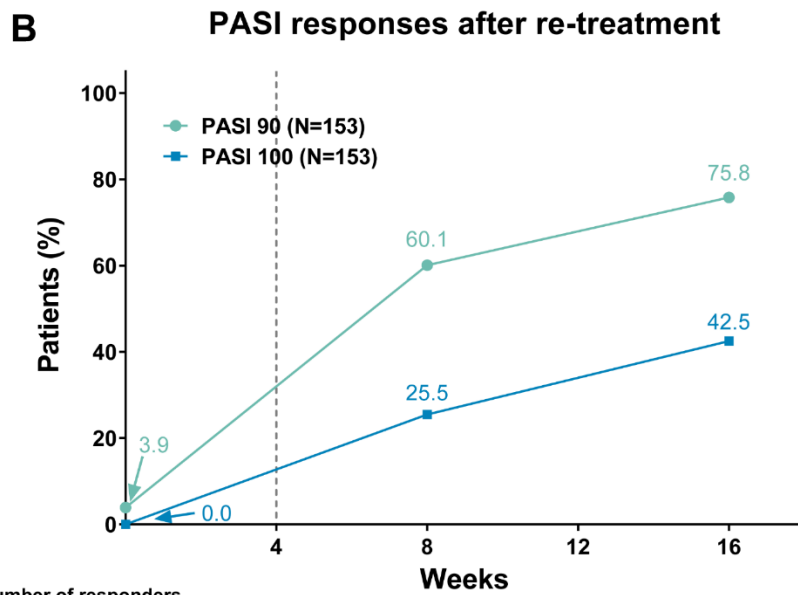
eFigure 7. Time to loss of PASI 90 after re-randomized to either continuous risankizumab or treatment withdrawal to placebo.
PASI=Psoriasis Area and Severity Index.

A

sPGA responses after re-treatment

Number of responders

sPGA 0/1	1	115	128
sPGA 0	0	39	64

B

PASI responses after re-treatment

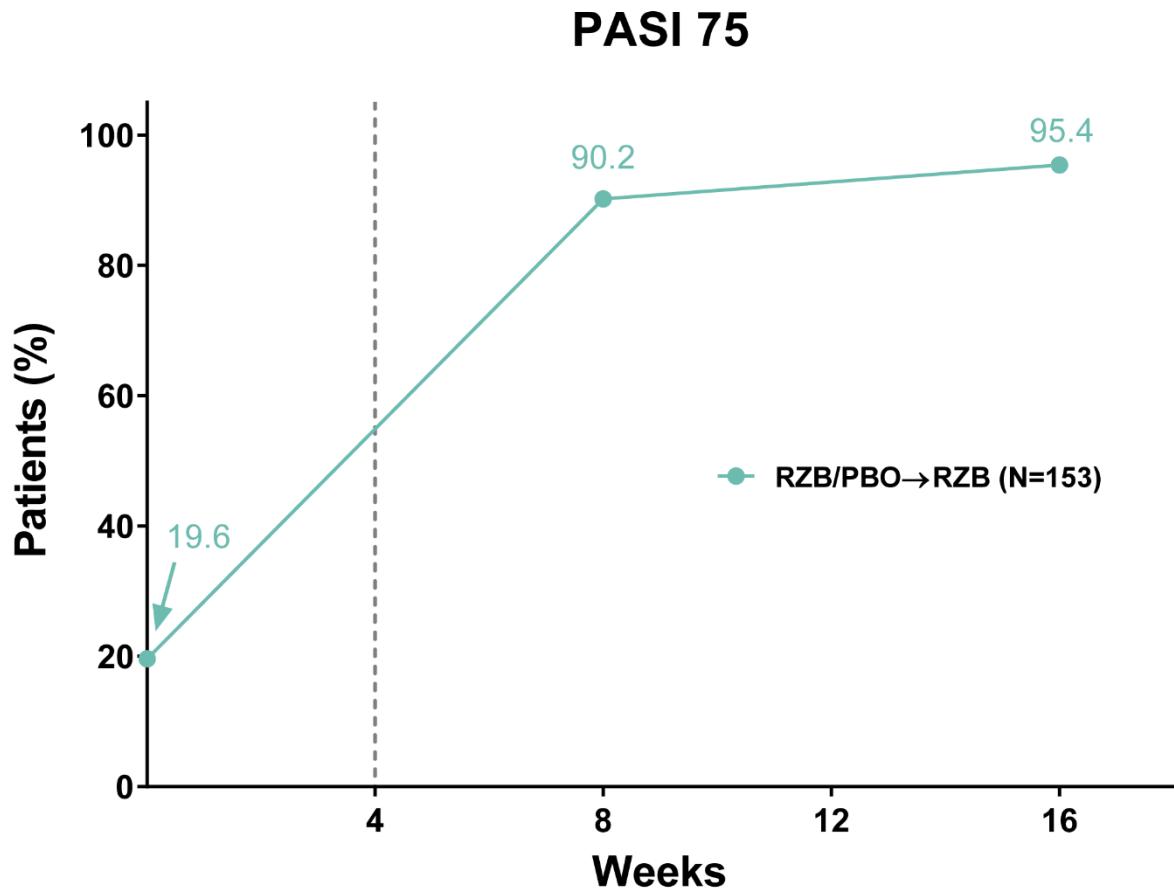Number of responders

PASI 90	6	92	116
PASI 100	0	39	65

eFigure 8. Proportion of patients (non-responder imputation) achieving sPGA (A) and PASI (B) responses after relapse during withdrawal and then re-treatment with risankizumab.

PASI=Psoriasis Area and Severity Index. sPGA=static Physician's Global Assessment.

PASI 75

Number of responders

PASI 75	30	138	146

eFigure 9. Proportion of patients (non-responder imputation) achieving PASI 75 responses after relapse during withdrawal and then re-treatment with risankizumab. Dotted line indicates risankizumab dose after an initial dose was given at week 0. PASI=Psoriasis Area and Severity Index.

eReferences

1. Simpson MJ, Chow C, Morgenstern H, Luger TA, Ellis CN. Comparison of three methods for measuring psoriasis severity in clinical studies (Part 2 of 2): use of quality of life to assess construct validity of the Lattice System Physician's Global Assessment, Psoriasis Area and Severity Index and Static Physician's Global Assessment. *J. Eur. Acad. Dermatol. Venereol.* 2015;29(7):1415-1420.

2. Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. *Ann. Rheum. Dis.* 2005;64(suppl 2):ii65-68; discussion ii69-73.

3. Weisman S, Pollack CR, Gottschalk RW. Psoriasis disease severity measures: comparing efficacy of treatments for severe psoriasis. *J Dermatolog Treat.* 2003;14(3):158-165.

4. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. *Clin. Exp. Dermatol.* 1994;19(3):210-216.