Supplementary file

Effectiveness and Safety of Secukinumab for Psoriasis in a Real-world Clinical Setting in the Asia-Pacific and Middle East regions: Results from the REALIA Study

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Inclusion criteria

1. Patients aged ≥ 18 years, able and willing to provide written informed consent
2. Patients with chronic plaque psoriasis diagnosed by a dermatologist
3. Patients with active skin lesions requiring treatment at baseline
4. Patients eligible for treatment with biologic agents or conventional systemic therapies (due primarily to their active skin lesions in the case of joint involvement) in compliance with the local prescribing information
5. Patients starting treatment with a biologic agent or a conventional systemic therapy for their condition at baseline, which included:
    a. Conventional systemics or biologic agents (incl. secukinumab) treatment-naïve patients starting a new treatment for chronic plaque psoriasis at baseline
    or
    b. Conventional systemics or biologic agents (incl. secukinumab) treatment experienced patients restarting a conventional systemics and/or biologic agents treatment after being untreated for at least 6 months
    or
    c. Patients switching to a different conventional systemics and/or biologic agent treatment (treatments that were already used in the past are allowed
    or
    d. Patients treated with conventional systemics requiring secukinumab or any other biologic agent as an add-on therapy

Exclusion criteria

Exclusion were contraindications to the prescribed biologic or conventional systemic agents in accordance with the local prescribing information, patients with almost clear or clear skin at baseline, patients being treated with secukinumab or any other biologics and administered conventional systemics as an add-on therapy at baseline and current or planned participation in an interventional clinical trial (including patients within the safety follow-up phase of a previous interventional study).

Details about statistical analysis

The FAS3, FAS6, and FAS12 were used for all the analyses related to effectiveness parameters, and ENS was used to report disposition. The EXS was used to analyse prior and concomitant psoriasis treatment, reasons for change in psoriasis treatment, AE reporting and other related safety parameters.

The primary objective was to investigate the magnitude of the difference in proportions, i.e., the risk difference (RD), for the following pairwise baseline treatment cohort comparisons of interest:

- secukinumab vs. conventional systemics
- Other biologics vs. conventional systemics

The RD along with the respective Wald asymptotic 95% confidence interval (CI) were calculated based on the number and percentage of patients achieving almost clear to clear skin at Month 3 (for FAS3), Month 6 (for FAS6) and Month 12 (for FAS12) for each baseline treatment cohort. The difference between baseline treatment cohorts in mean change from baseline PASI, BSA and DLQI total scores at Month 3, Month 6 and Month 12 was based on a mixed model repeated measures (MMRM) analysis for FAS3, FAS6 and FAS12 for data up to and including Month 3, Month 6 and Month 12, respectively. All safety analyses were performed on the EXS.

Change in BSA total score from baseline

SEC patients showed significantly higher change in BSA total score from baseline vs. CS at Month 3 (LS mean [SE]: −23.18 [1.514] vs. −10.23 [2.361], P<0.001) and Month 12 (LS mean [SE]: −22.46 [1.296] vs. −15.30 [2.192], *P*=0.004) (Supplementary Figure 1). Similarly, BIO patients showed significantly higher change in BSA total score from baseline (LS mean [SE]: −19.97 [1.155] *P*<0.001) at Month 3 and Month 12 (LS mean [SE]: −20.49 [1.140], *P*=0.033) vs. CS.

Health-related quality of life

SEC patients showed significantly higher change in DLQI total score from baseline vs. CS at Month 3 (LS mean [SE]: −10.49 [0.667] vs. −6.60 [0.814], *P*<0.001) and Month 12 (LS mean [SE]: −10.99 [0.721] vs. −8.18 [0.907], *P*=0.011) (Supplementary Figure 1). BIO patients showed significantly higher change in DLQI total score from baseline at Month 3 (LS mean [SE]: −9.43 [0.641], *P*=0.004) and numerically higher change at Month 12 (LS mean [SE]: −9.40 [0.698], P=0.257) vs. CS (Supplementary Figure 1).

SUPPLEMENTARY TABLES AND FIGURES

Supplementary table S1. Proportion of patients not meeting eligibility criteria

Treatment cohort	All patients (N=554), n (%)
Subjects not treated (eligibility criteria not met)	**13 (2.3)**
Any exclusion criteria met	**4 (0.7)**
Contraindications to the prescribed biologic or conventional systemic agents in accordance with the local prescribing information	1 (0.2)
Patients being treated with secukinumab or any other biologic agents and administered conventional systemics as an add-on therapy at Baseline	1 (0.2)
Patients with almost clear or clear skin at Baseline	2 (0.4)
Any inclusion criteria not met	**9 (1.6)**
Patients aged ≥18 years, able and willing to provide written informed consent	1 (0.2)
Patients starting treatment with a biologic agent or a conventional systemic therapy for their condition at baseline	6 (1.1)
Patients with chronic plaque psoriasis diagnosed by a dermatologist	2 (0.4)

N: total number of patients; n: number of patients

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Supplementary table S2. Prior psoriasis treatment (EXS, baseline treatment cohort)

Psoriasis Therapy	Conventional systemics (N=173), n (%)	Secukinumab (N=184), n (%)	Other biologics (N=184), n (%)	Total (N=541), n (%)
Chronic plaque psoriasis prior treatment characteristics				
Topical treatment				
Yes	165 (95.4)	176 (95.7)	174 (94.6)	515 (95.2)
No	7 (4.0)	6 (3.3)	10 (5.4)	23 (4.3)
Unknown	1 (0.6)	2 (1.1)	0	3 (0.6)
Phototherapy				
Yes	69 (39.9)	107 (58.2)	105 (57.1)	281 (51.9)
No	102 (59.0)	74 (40.2)	77 (41.8)	253 (46.8)
Unknown	2 (1.2)	3 (1.6)	2 (1.1)	7 (1.3)
Conventional systemic therapy (including PUVA)				
Yes	63 (36.4)	137 (74.5)	126 (68.5)	326 (60.3)
No	109 (63.0)	46 (25.0)	58 (31.5)	213 (39.4)
Unknown	1 (0.6)	1 (0.5)	0	2 (0.4)
Biologic agent				
Yes	9 (5.2)	82 (44.6)	58 (31.5)	149 (27.5)
No	163 (94.2)	102 (55.4)	124 (67.4)	389 (71.9)
Unknown	1 (0.6)	0	2 (1.1)	3 (0.6)
Chronic plaque psoriasis prior biologic characteristics				

Experience ≥2 biologic agents[a]				
Yes	2 (1.2)	43 (23.4)	16 (8.7)	61 (11.3)
No	7 (4.0)	39 (21.2)	42 (22.8)	88 (16.3)
Reason for discontinuation of previous biologic[b]				
Treatment cost	5 (2.9)	14 (7.6)	21 (11.4)	40 (7.4)
Lack of efficacy	2 (1.2)	57 (31.0)	24 (13.0)	83 (15.3)
Safety/tolerability	1 (0.6)	3 (1.6)	7 (3.8)	11 (2.0)
Pregnancy	0	0	2 (1.1)	2 (0.4)
Unknown	0	7 (3.8)	6 (3.3)	13 (2.4)
Disease improvement	0	10 (5.4)	4 (2.2)	14 (2.6)
Other	2 (1.2)	5 (2.7)	6 (3.3)	13 (2.4)
Baseline concomitant psoriasis medications				
Topical treatment	144 (83.2)	95 (51.6)	113 (61.4)	352 (65.1)
Phototherapy (including PUVA)	46 (26.6)	10 (5.4)	14 (7.6)	70 (12.9)

[a]Response based on 149 patients who received prior biologics. [b]Patients may have more than one reason for discontinuation. Percentages are based on the number of patients in the EXS for each respective baseline treatment cohort. EXS: exposed set; N: total number of patients; n: number of patients

Supplementary table S3. Baseline treatment cohort (EXS)

Treatment cohort	Conventional systemics (N=173), n (%)	Secukinumab (N=184), n (%)	Other biologics (N=184), n (%)	Total (N=541), n (%)
Conventional systemics	173 (100.0)	16 (8.7)	29 (15.8)	218 (40.3)
Acitretin	34 (19.7)	6 (3.3)	8 (4.3)	48 (8.9)
Apremilast	3 (1.7)	0	0	3 (0.6)
Cyclosporine	21 (12.1)	5 (2.7)	3 (1.6)	29 (5.4)
Methotrexate	117 (67.6)	6 (3.3)	18 (9.8)	141 (26.1)
Secukinumab	0	184 (100.0)	0	184 (34.0)
Other biologics	0	1 (0.5)	184 (100.0)	185 (34.2)
Adalimumab	0	0	41 (22.3)	41 (7.6)
Etanercept	0	0	11 (6.0)	11 (2.0)
Guselkumab	0	0	2 (1.1)	2 (0.4)
Infliximab	0	0	2 (1.1)	2 (0.4)
Ixekizumab	0	0	32 (17.4)	32 (5.9)
Tildrakizumab	0	0	4 (2.2)	4 (0.7)
Ustekinumab	0	1 (0.5)[a]	92 (50.0)	93 (17.2)

Patients in secukinumab or other biologics cohort could also have received conventional systemics. [a]One patient (0.5%) received ustekinumab in combination with secukinumab at baseline. Percentages are based on the number of patients in the EXS for each respective baseline treatment cohort. EXS: exposed set; N: total number of patients; n: number of patients

Supplementary table S4. Actual treatment cohort (EXS)

Treatment cohort	Conventional systemics (N=182), n (%)	Secukinumab (N=211), n (%)	Other biologics (N=213), n (%)
Conventional systemics	182 (100.0)	31 (14.7)	47 (22.1)
Acitretin	45 (24.7)	12 (5.7)	11 (5.2)
Apremilast	3 (1.6)	0	1 (0.5)
Azathioprine	1 (0.5)	0	1 (0.5)
Cyclosporine	30 (16.5)	8 (3.8)	6 (2.8)
Methotrexate	136 (74.7)	13 (6.2)	30 (14.1)
Secukinumab	0	211 (100.0)	0
Other biologics	0	5 (2.4)	213 (100.0)
Adalimumab	0	2 (0.9)	50 (23.5)
Etanercept	0	1 (0.5)	14 (6.6)
Guselkumab	0	0	13 (6.1)
Infliximab	0	0	4 (1.9)
Ixekizumab	0	0	43 (20.2)
Tildrakizumab	0	0	6 (2.8)
Ustekinumab	0	2 (0.9)	101 (47.4)

Patients in secukinumab or other biologics cohort could also have received conventional systemics. Percentages are based on the number of patients in the EXS for each respective actual treatment cohort. EXS: exposed set; N: total number of patients; n: number of patients

Supplementary table S5. Primary reason for change of treatment including treatment regimen (EXS, baseline treatment cohort)

Primary reason for change	Conventional systemics (N=173), n (%)			Secukinumab (N=184), n (%)			Other biologics (N=184), n (%)		
Month (m)	**3 (114)**	**6 (73)**	**12 (100)**	**3 (133)**	**6 (125)**	**12 (130)**	**3 (122)**	**6 (109)**	**12 (125)**
Treatment convenience	0	2 (2.7)	0	0	1 (0.8)	0	1 (0.8)	0	0
Cost	0	1 (1.4)	2 (2.0)	0	0	0	0	0	0
Disease improvement	7 (6.1)	3 (4.1)	6 (6.0)	10 (7.5)	3 (2.4)	0	21 (17.2)	4 (3.7)	3 (2.4)
Unsatisfactory therapeutic response	17 (14.9)	13 (17.8)	13 (13.0)	5 (3.8)	4 (3.2)	12 (9.2)	9 (7.4)	12 (11.0)	9 (7.2)
Pregnancy	0	0	0	0	1 (0.8)	0	0	1 (0.9)	0
Safety/Tolerability	19 (16.7)	3 (4.1)	3 (3.0)	2 (1.5)	1 (0.8)	3 (2.3)	0	1 (0.9)	3 (2.4)
Other	5 (4.4)	2 (2.7)	3 (3.0)	4 (3.0)	2 (1.6)	8 (6.2)	3 (2.5)	0	2 (1.6)
Not reported	0	0	0	0	0	0	2 (1.6)	0	1 (0.8)

Patients may be assessed more than once at a visit. Percentages are based on the number of patients in the EXS with data available (m) at the visit of interest for each respective baseline treatment cohort. EXS: exposed set.

Supplementary file

FIGURES LEGENDS

Supplementary fig. S1. Adjusted mean change in BSA total score from baseline (baseline treatment cohort)

Error bars represent SE. Analysed using MMRM model including baseline treatment cohort, psoriatic arthritis, visit as fixed effect factors, baseline BSA total score value as covariate and the baseline treatment cohort by visit interaction, psoriatic arthritis by visit interaction, and baseline BSA total score by visit interaction. †other biologics vs conventional systemics; *secukinumab vs conventional systemics. BSA, body surface area; FAS3/6/12, full analysis set at Month 3, 6 or 12; LS: least-squares; MMRM: mixed model repeated measures; SE: standard error

Supplementary fig. S2. Adjusted mean change in DLQI total score from baseline (baseline treatment cohort)

Error bars represent SE. Analysed using MMRM model including baseline treatment cohort, psoriatic arthritis, visit as fixed effect factors, baseline DLQI total score value as covariate and the baseline treatment cohort by visit interaction, psoriatic arthritis by visit interaction, and baseline DLQI total score by visit interaction. †other biologics vs conventional systemics; *secukinumab vs conventional systemics. DLQI, Dermatology Life Quality Index; FAS3/6/12, full analysis set at Month 3, 6 or 12; LS: least-squares; MMRM: mixed model repeated measures; SE: standard error

Supplementary fig. S3. (i) Proportion of patients with a change in treatment regimen during the study; (ii) Type of change including treatment regimen during the study (EXS, baseline treatment cohort)

This figure summarises the number of changes in treatment since the last visit. The changes presented are summarised under each patient's original baseline treatment cohort. Percentages are based on the number of patients in the EXS in the respective baseline treatment cohort. EXS: exposed set; N: total number of patients.

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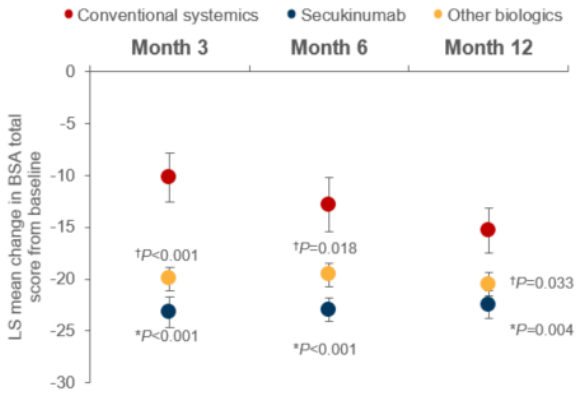
Supplementary fig. S4. Proportion of patients with a change of treatment including treatment regimen adjustment since the last visit (EXS, baseline treatment cohort)

Patients may be assessed more than once at a visit. Percentages are based on the number of patients in the EXS with data available (m) at the visit of interest for each respective baseline treatment cohort. EXS, exposed set; m: number of patients available for assessment; N: total number of patients.

Supplementary file

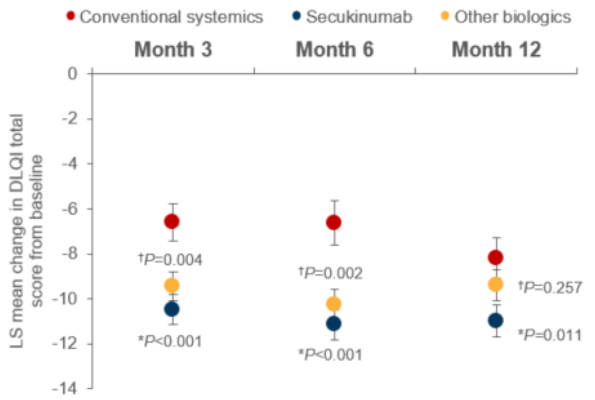
Supplementary fig. S1. Adjusted mean change in BSA total score from baseline (baseline treatment cohort)



	Number of patients with BSA total score available		
	Conventional systemics	Secukinumab	Other biologics
FAS3	50	48	74
FAS6	27	51	65
FAS12	29	45	64

Error bars represent SE. Analysed using MMRM model including baseline treatment cohort, psoriatic arthritis, visit as fixed effect factors, baseline BSA total score value as covariate and the baseline treatment cohort by visit interaction, psoriatic arthritis by visit interaction, and baseline BSA total score by visit interaction. †other biologics vs conventional systemics; *secukinumab vs conventional systemics. BSA, body surface area; FAS3/6/12, full analysis set at Month 3, 6 or 12; LS: least-squares; MMRM: mixed model repeated measures; SE: standard error

Supplementary fig. S2. Adjusted mean change in DLQI total score from baseline (baseline treatment cohort)



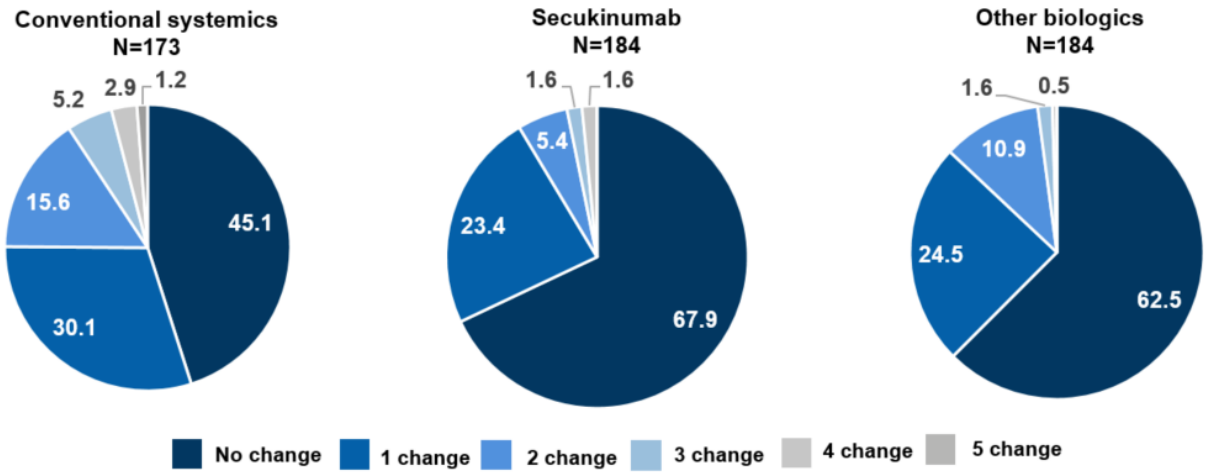
	Number of patients with DLQI total score available		
	Conventional systemics	Secukinumab	Other biologics
FAS3	81	80	101
FAS6	45	70	74
FAS12	49	63	80

Error bars represent SE. Analysed using MMRM model including baseline treatment cohort, psoriatic arthritis, visit as fixed effect factors, baseline DLQI total score value as covariate and the baseline treatment cohort by visit interaction, psoriatic arthritis by visit interaction, and baseline DLQI total score by visit interaction. †other biologics vs conventional systemics; *secukinumab vs conventional systemics. DLQI, Dermatology Life Quality Index; FAS3/6/12, full analysis set at Month 3, 6 or 12; LS: least-squares; MMRM: mixed model repeated measures; SE: standard error

Supplementary file

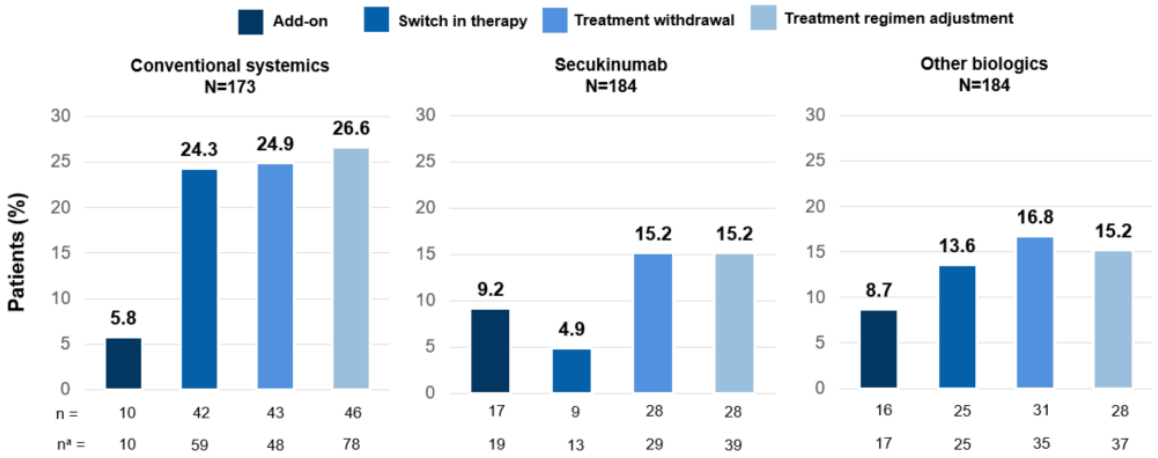
Supplementary fig. S3. (i) Proportion of patients with a change in treatment regimen during the study; (ii) Type of change including treatment regimen during the study (EXS, baseline treatment cohort)

i



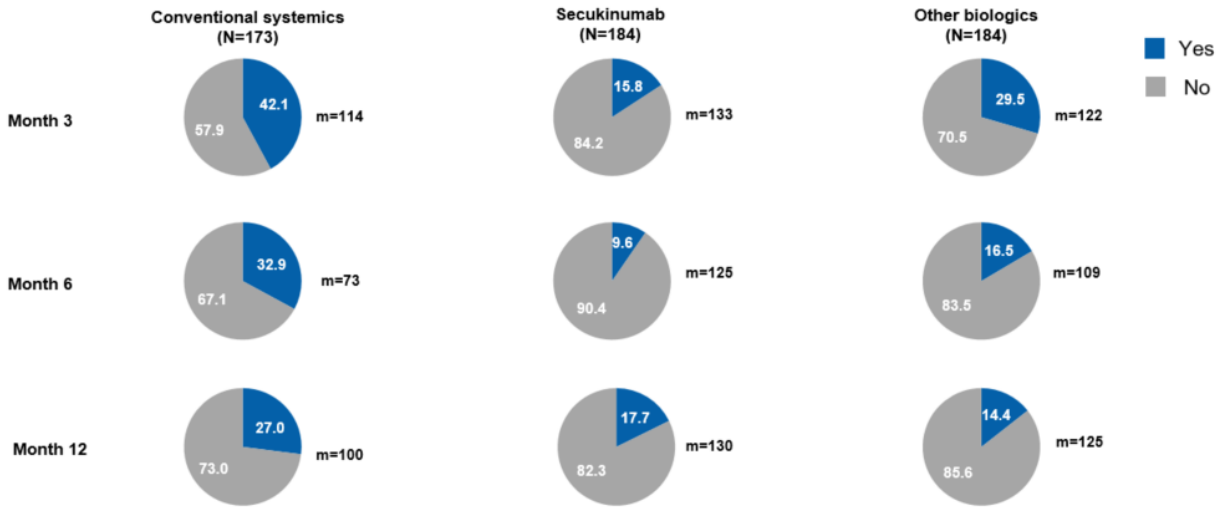
This figure summarises the number of changes in treatment since the last visit. The changes presented are summarised under each patient's original baseline treatment cohort. Percentages are based on the number of patients in the EXS in the respective baseline treatment cohort. EXS: exposed set; N: total number of patients.

ii



Supplementary file

Supplementary fig. S4. Proportion of patients with a change of treatment including treatment regimen adjustment since the last visit (EXS, baseline treatment cohort)



Patients may be assessed more than once at a visit. Percentages are based on the number of patients in the EXS with data available (m) at the visit of interest for each respective baseline treatment cohort. EXS, exposed set; m: number of patients available for assessment; N: total number of patients.