Supplementary Materials for
Baseline characteristics and mNAPSI change from baseline scores through month 12 for patients with moderate-to-severe plaque psoriasis and concomitant nail psoriasis treated with biologics from PSoHO

Elisabeth Riedl[1], Andreas Pinter[2], Shirin Zaheri[3], Antonio Costanzo[4,5], Alan Brnabic[6], Bruce Konicek[6], Robert McKenzie[6], Anastasia Lampropoulou[6], Mohamed El Rayes[6], Natalie Haustrup[6]*, Christopher Schuster[1,6]*
*contributed equally

[1]Department of Dermatology, Medical University of Vienna, Vienna, Austria;

[2]University Hospital Frankfurt, Frankfurt am Main, Germany;

[3]Department of Dermatology, The Harley Street Clinic, HCA Healthcare UK, London, UK;

[4]Division of Dermatology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy;

[5]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy;

[6]Eli Lilly and Company, Indianapolis, USA;

Supplementary Figures:
> **Figure S1:** Sensitivity analysis of data with missing data imputed using Last Observation Carried Forward (LOCF).
> **Figure S2:** Comparison of biologics using mNAPSI change from baseline for EMA on-label population.
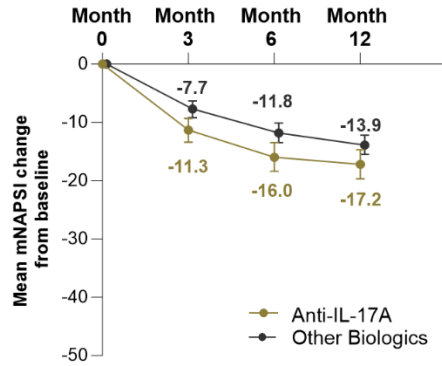
Statistical Appendix

> **Supplementary text**

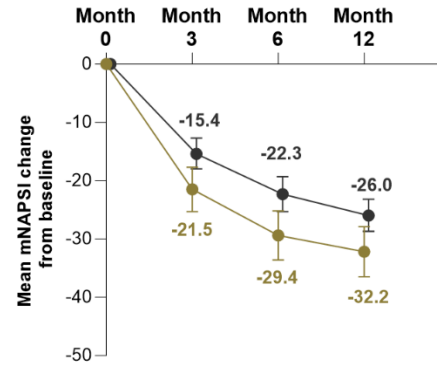> **Table S1:** List of covariates used in FMA adjusted analyses.

> **Table S2:** List of reduced number of covariates used for FMA adjusted analyses with small sample sizes.
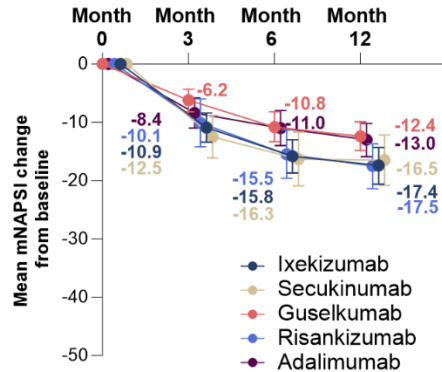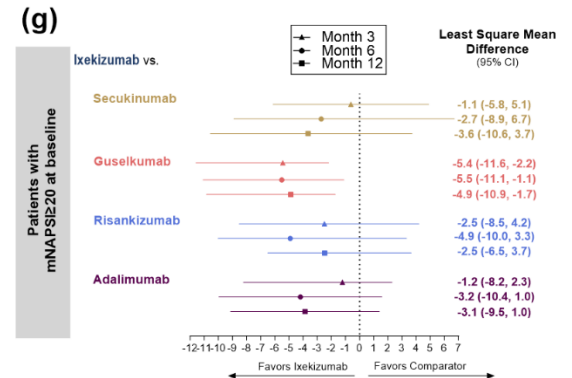
Figure S1: Sensitivity analysis comparing biologics using mean mNAPSI change from baseline. For unadjusted and adjusted results, missing data were imputed using Last Observation Carried Forward (LOCF). **(a)** patients with mNAPSI≥1 at baseline in the anti-IL-17A cohort

and other biologics cohort; **(b)** patients with mNAPSI≥20 at baseline in the anti-IL-17A cohort and other biologics cohort; **(c)** adjusted least square mean difference comparisons of anti-IL-17A cohort with other biologics cohort for patients with mNAPSI≥1 or mNAPSI≥20 at baseline; **(d)** patients with mNAPSI≥1 at baseline in IXE, SEC, GUS, RIS and ADA treatment groups; **(e)** patients with mNAPSI≥20 at baseline in IXE, SEC, GUS, RIS and ADA individual treatmen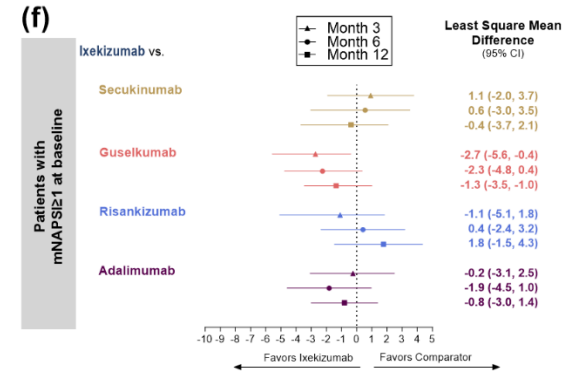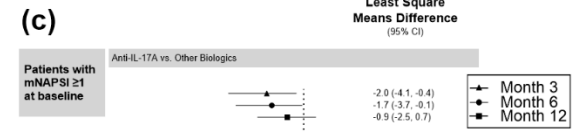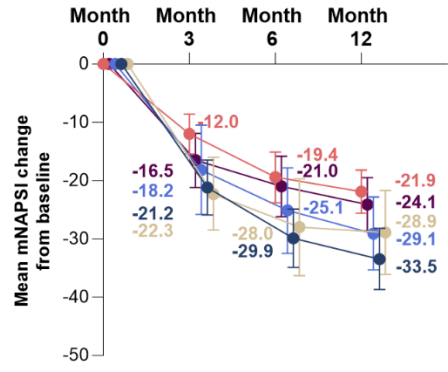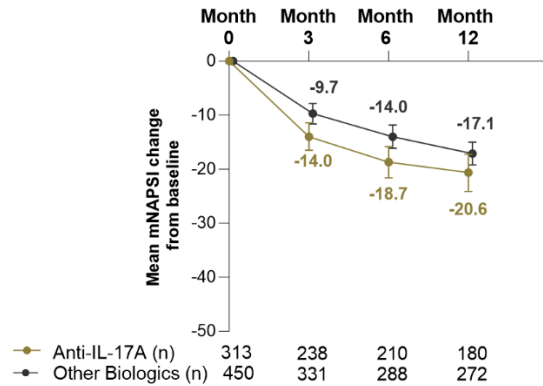t groups; **(f)** adjusted least square mean difference comparisons of IXE vs. 4 other individual biologics for patients with mNAPSI≥1 at baseline **(g)** adjusted least square mean difference comparisons of IXE vs. 4 other individual biologics for patients with mNAPSI≥20 at baseline. In adjusted analyses, the result is significant if the confidence intervals do not cross 0. The number of patients with mNAPSI≥1 in the anti-IL-17A cohort is 313 and in the other biologics cohort is 450. The number of patients with mNAPSI≥20 in the anti-IL-17A cohort is 142 and in the other biologics cohort is 200. The number of patients with mNAPSI≥1 receiving ixekizumab is 230, secukinumab is 83, guselkumab is 117, risankizumab is 91, and adalimumab is 106. The number of patients with mNAPSI≥20 receiving ixekizumab is 103, secukinumab is 39, guselkumab is 54, risankizumab is 44, and adalimumab is 45. ADA, adalimumab; GUS, guselkumab; IL-17A, interleukin-17A; IXE, ixekizumab; LSMD, least square mean difference; mNAPSI, modified Nail Psoriasis Severity Index; n, number of patients; RIS, risankizumab; SEC, secukinumab.

Patients who received EMA on-label dosing

(a) Patients with mNAPSI≥1

Mean mNAPSI change from baseline

	Month 0	Month 3	Month 6	Month 12
Other Biologics	0	-9.7	-14.0	-17.1
Anti-IL-17A	0	-14.0	-18.7	-20.6

Anti-IL-17A (n)	313	238	210	180
Other Biologics (n)	450	331	288	272

(b) Patients with mNAPSI≥20

Mean mNAPSI change from baseline

	Month 0	Month 3	Month 6	Month 12
Other Biologics	0	-18.7	-24.7	-29.0
Anti-IL-17A	0	-26.7	-33.2	-38.6

	142	108	99	82
	200	151	134	131

(c) Least Square Means Difference (95% CI)

Anti-IL-17A vs. Other Biologics

Patients with mNAPSI ≥1 at baseline
- Month 3: -2.7 (-4.2, -0.8)
- Month 6: -2.4 (-4.4, -0.7)
- Month 12: -1.3 (-2.8, 0.7)

Patients with mNAPSI ≥20 at baseline
- Month 3: -3.5 (-7.8, -0.4)
- Month 6: -3.3 (-7.2, -0.3)
- Month 12: -2.5 (-5.5, -0.3)

← Favors Anti-IL-17A   Favors Other Biologics →

(d) Patients with mNAPSI≥1

Mean mNAPSI change from baseline

	Week 0	Month 3	Month 6	Month 12
GUS	0	-7.3	-12.0	-12.7
ADA	0	-12.3	-13.9	-16.1
RIS	0	-12.4	-16.6	-19.0
IXE	0	-13.3	-18.2	-20.6
SEC	0	-16.0	-20.4	-20.8

	Week 0	Month 3	Month 6	Month 12
IXE (n)	230	177	159	136
SEC (n)	83	61	51	44
GUS (n)	117	96	82	79
RIS (n)	91	68	69	63
ADA (n)	106	70	58	52

(e) Patients with mNAPSI≥20

Mean mNAPSI change from baseline

	Month 0	Month 3	Month 6	Month 12
GUS	0	-13.6	-20.0	-20.9
RIS	0	-20.6	-25.9	-28.6
ADA	0	-24.7	-26.8	-28.4
IXE	0	-26.4	-33.0	-38.9
SEC	0	-27.4	-33.8	-37.8

	Month 0	Month 3	Month 6	Month 12
	103	77	73	61
	39	31	26	21
	54	46	42	39
	44	36	34	34
	45	29	23	21

(f) Least Square Mean Difference (95% CI)

Patients with mNAPSI≥1 at baseline

Ixekizumab vs.

Secukinumab
- Month 3: -0.3 (-3.3, 2.7)
- Month 6: 0.5 (-1.7, 3.1)
- Month 12: -0.3 (-3.5, 2.3)

Guselkumab
- Month 3: -4.8 (-7.5, -2.8)
- Month 6: -5.0 (-7.5, -2.6)
- Month 12: -3.1 (-5.6, -1.5)

Risankizumab
- Month 3: -2.9 (-5.9, 1.0)
- Month 6: -1.1 (-3.9, -1.4)
- Month 12: -0.6 (-3.2, 1.8)

Adalimumab
- Month 3: 1.4 (-1.5, 3.9)
- Month 6: 0.2 (-1.6, 2.8)
- Month 12: 0.6 (-2.2, 3.5)

← Favors Ixekizumab   Favors Comparator →

(g) Least Square Mean Difference (95% CI)

Patients with mNAPSI≥20 at baseline

Ixekizumab vs.

Secukinumab
- Month 3: -3.1 (-8.6, 3.3)
- Month 6: 0.0 (-4.5, 5.6)
- Month 12: -1.8 (-7.8, 3.7)

Guselkumab
- Month 3: -7.3 (-13.0, -4.2)
- Month 6: -7.6 (-11.7, -2.6)
- Month 12: -8.5 (-12.9, -4.3)

Risankizumab
- Month 3: -4.8 (-12.6, 2.4)
- Month 6: -7.7 (-13.3, -0.9)
- Month 12: -5.1 (-8.8, -1.0)

Adalimumab
- Month 3: 4.3 (-0.7, 7.6)
- Month 6: 2.8 (-3.2, 7.8)
- Month 12: -3.2 (-7.3, 4.5)

← Favors Ixekizumab   Favors Comparator →

Figure S2: Comparison of biologics using mean mNAPSI change from baseline for the EMA on-label population (as observed): (a)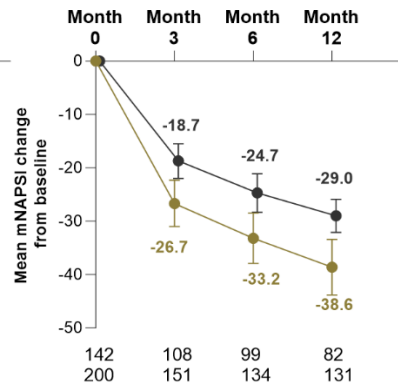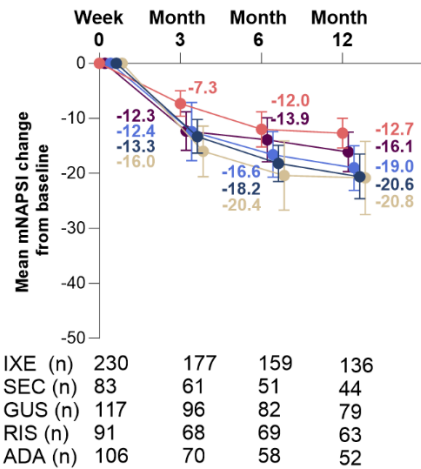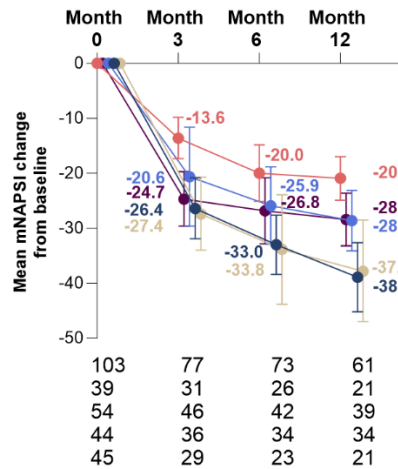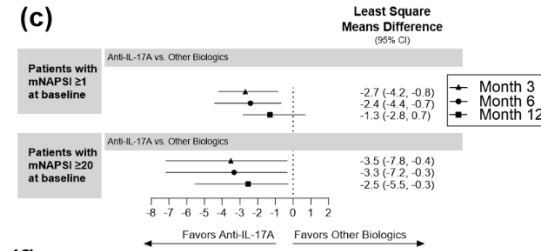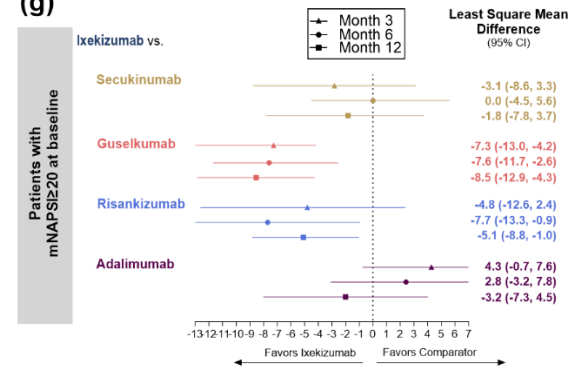 patients with mNAPSI≥1 at baseline in the anti-IL-17A cohort and other biologics cohort; **(b)** patients with mNAPSI≥20 at baseline in the anti-IL-

17A cohort and other biologics cohort; **(c)** adjusted comparisons of anti-IL-17A cohort with other biologics cohort for patients with mNAPSI≥1 or mNAPSI≥20 at baseline; **(d)** patients with mNAPSI≥1 at baseline in IXE, SEC, GUS, RIS and ADA treatment groups; **(e)** patients with mNAPSI≥20 at baseline in IXE, SEC, GUS, RIS and ADA individual treatment groups; **(f)** adjusted least square mean difference comparisons of IXE vs. 4 other individual biologics for patients with mNAPSI≥1 at baseline **(g)** adjusted least square mean difference comparisons of IXE vs. 4 other individual biologics for patients with mNAPSI≥20 at baseline. Data are presented as observed. In adjusted analyses, the result is significant if the confidence intervals do not cross 0. Due to small sample sizes of treatment groups with patients with mNAPSI≥20 at baseline, the majority of models did not converge at months 6 and 12, therefore Figure S2g FMA analyses employed a reduced number of variables at months 6 and 12. Tables report assigned patient numbers for each treatment at baseline and number of patients receiving EMA on-label dosing with mNAPSI results at respective visits.

ADA, adalimumab; EMA, European Medicines Agency; GUS, guselkumab; IL-17A, interleukin-17A; IXE, ixekizumab; LSMD, least square mean difference; mNAPSI, modified Nail Psoriasis Severity Index; n, number of patients; RIS, risankizumab; SEC, secukinumab.

Statistical Appendix

Baseline covariates for adjusted analyses

Adjusted comparisons of biologics and class cohorts applied the same frequentist model averaging (FMA) methodology and adjusted for the same covariates as per other recently published PSoHO analyses[1-3]. In brief, PSoHO used real-world data and applied comparative analysis in a causal inference FMA framework based on machine learning. Treatment models balanced the treatment groups by generating a propensity score using either logistic regression or gradient boosting models with covariates selected based on penalized regression models (lasso or elastic net). Outcome models included generalized linear regression, penalized regression, the greedy matching algorithm or inverse probability treatment weighting regression.

Table S1 provides the full list of covariates that models were adjusted for. Where small sample sizes resulted in the non-convergence of the majority of models, a reduced number of variables were employed, as listed in Table S2. All analyses were conducted using SAS 9.4 and R Version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Table S1: List of covariates used in FMA adjusted analyses.

At baseline		
Patient demographics	**Selected comorbidities associated with psoriasis**	**Patient disease characteristics**
Age	Diabetes Mellitus	Number of comorbidities
Sex	Inflammatory bowel disease	Baseline PASI score
BMI	Ankylosing spondylitis (AS) and Axial AS	Baseline sPGA score
Smoking status	Obesity	Baseline BSA score
Duration of disease	Overweight	Baseline Itch VAS score
Biologic experience	Dyslipidemia	Baseline Skin VAS score
Family history of psoriasis	PsA	Psoriasis visible on areas of:
Previous phototherapy	Rheumatic disease unrelated to PsO/PsA	• the face and/or neck
Previous psoriasis systemic treatments	Other comorbidities associated with psoriasis	• the scalp
Concomitant treatment		• the palms and/or soles
Current psoriasis treatment		• the genital area
		Baseline mNAPSI score
		Baseline WPAI-PSO Score
		Percent activity impairment due to all health
		Baseline DLQI score
		Baseline HADS score (total/anxiety/depression)
		Medication Adherence Reporting Scale (MARS-5)
		Psoriasis Symptoms and Signs Diary (PSSD)

AS, Ankylosing spondylitis; BSA, Body Surface Area; DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; mNAPSI, modified Nail Psoriasis Severity Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; PSSD, Psoriasis Symptoms and Signs Diary; sPGA, static Physician's Global Assessment; VAS, visual analog scale; WPAI-PSO, Work Productivity and Activity Impairment Questionnaire - Psoriasis.

Table S2: List of reduced number of covariates used in FMA adjusted analyses when small sample sizes led to lack of model convergence.

At baseline		
Patient demographics	**Selected comorbidities associated with psoriasis**	**Patient disease characteristics**
Age Sex BMI Duration of disease Biologic experience Family history of psoriasis Previous psoriasis systemic treatments	PsA	Baseline PASI score Baseline mNAPSI score Baseline DLQI score

References

1   Pinter A, Costanzo A, Khattri S *et al.* Comparative Effectiveness and Durability of Biologics in Clinical Practice: Month 12 Outcomes from the International, Observational Psoriasis Study of Health Outcomes (PSoHO). *Dermatology and Therapy* 2023.

2   Pinter A, Puig L, Schäkel K *et al.* Comparative Effectiveness of Biologics in Clinical Practice: Week 12 Primary Outcomes from an International Observational Psoriasis Study of Health Outcomes (PSoHO). *J Eur Acad Dermatol Venereol* 2022.

3   Piaserico S, Riedl E, Pavlovsky L *et al.* Comparative effectiveness of biologics for patients with moderate-to-severe psoriasis and special area involvement: week 12 results from the observational Psoriasis Study of Health Outcomes (PSoHO). *Frontiers in Medicine* 2023; **10**.