Supplementary material to article by J. H. O. Hoffmann et al. "Evaluation of Psoriasis Area and Severity Index as a Proxy for Biomarkers of Systemic Disease under Treatment with Tumour Necrosis Factor-alpha and Interleukin 12/23 Antagonists in Patients with Psoriasis: A Retrospective Cohort Study of 186 Treatment Cycles"

## Appendix S1

## SUPPLEMENTARY RESULTS

Significant correlation of Psoriasis Area and Severity Index with C-reactive protein, neutrophil and leucocyte count, and neutrophil-to-lymphocyte ratio

Psoriasis Area and Severity Index (PASI) was significantly correlated with C-reactive protein (CRP), neutrophil counts, and neutrophil-to-lymphocyte ratio (NLR) in the entire study population using all available data points (Table II).

A subgroup Spearman's rank-correlation analysis of patients without concomitant methotrexate treatment did not show a significant correlation between PASI and transaminases (glutamate-oxaloacetate transaminase, glutamate-pyruvate transaminase and  $\gamma$ -glutamyl transaminase: Spearman's correlation coefficient 0.085, 0.086, 0.112, p=0.285, 0.280, 0.159, respectively; all n=160). The Spearman's correlation coefficients of PASI with CRP and NLR in biologic-naïve patients were similar to the correlation coefficients of 0.262 and 0.223, respectively, in the entire study population (PASI-CRP biologic naïve:  $r_s=0.302$ , p=0.001, n=110; PASI-NLR biologic naïve:  $r_s=0.235$ , p=0.014, n=110).

The median NLR and CRP under treatment were significantly lower in patients with vs without a median PASI 75 response (NLR: 1.8 vs 2.2, n=69 vs 106, p=0.031; CRP: 2.0 vs 2.4, n=69 vs 106, p<0.001, Mann–Whitney U test, **SFig. 1**). Median NLR and CRP under treatment in patients with vs without a median PASI 100 response were 1.8 vs 2.1 (n=20 vs 155, p=0.178) and 2.0 [IQR 2, 2] vs 2.0 [IQR 2, 4] (n=20 vs 155, p=0.011), respectively. Median NLR and CRP under treatment in patients with psoriasis arthritis were 2.0 vs 2.1 (n=99 vs 86, p=0.076) and 2.0 [IQR 2, 4] vs 2.0 [IQR 2, 5] (n=99 vs 86, p=0.205, all Mann–Whitney U tests), respectively.

## Neutrophil-to-lymphocyte ratio and C-reactive protein are associated with Psoriasis Area and Severity Index independent of each other and treatment duration

To further assess the effects of treatment duration, we performed subgroup correlation analyses of PASI with CRP and NLR limited to data from the first 3 months,



SFig. 1. Neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) under treatment stratified according to Psoriasis Area and Severity Index (PASI) 75 response. (A) Median NLR and (B) CRP concentrations were significantly lower in patients who achieved, a median of, at least a 75% improvement in their PASI compared with baseline (PASI 75).

3–12 months and later than 12 months. The Spearman's rank correlation coefficients of PASI with CRP were similar in all 3 periods and the correlation coefficient of PASI with NLR did not demonstrate a clear relationship with treatment duration (PASI-CRP: 0.203, 0.247, and 0.277 for the first 3 months, 3–12 months and later than 12 months; PASI-NLR: 0.110, 0.221, 0.149 for the first 3 months, 3–12 months and later than 12 months; 0.12 months and later than 12 months.

CRP was significantly correlated with treatment duration (cf main Results section). The reduction of CRP was most pronounced during the first 3 months of treatment (Spearman's correlation coefficient between CRP and treatment duration:  $r_s$ : -0.148, p=<0.001). The correlation was less pronounced at later time-points (>3 months: -0.080, p=0.001, >6 months: -0.081, p=0.002, >12 months: -0.049, p=0.111).

## Inter-individual spread of the correlation of PASI with neutrophil-to-lymphocyte ratio and C-reactive protein

Previous biologic treatments did not significantly predict a strong (Spearman's correlation coefficient >0.5) PASI-CRP nor PASI-NLR correlation (Exp (B): 0.976, p=0.915, and Exp (B): 0.821, p=0.346, respectively; univariate logistic regression analysis).