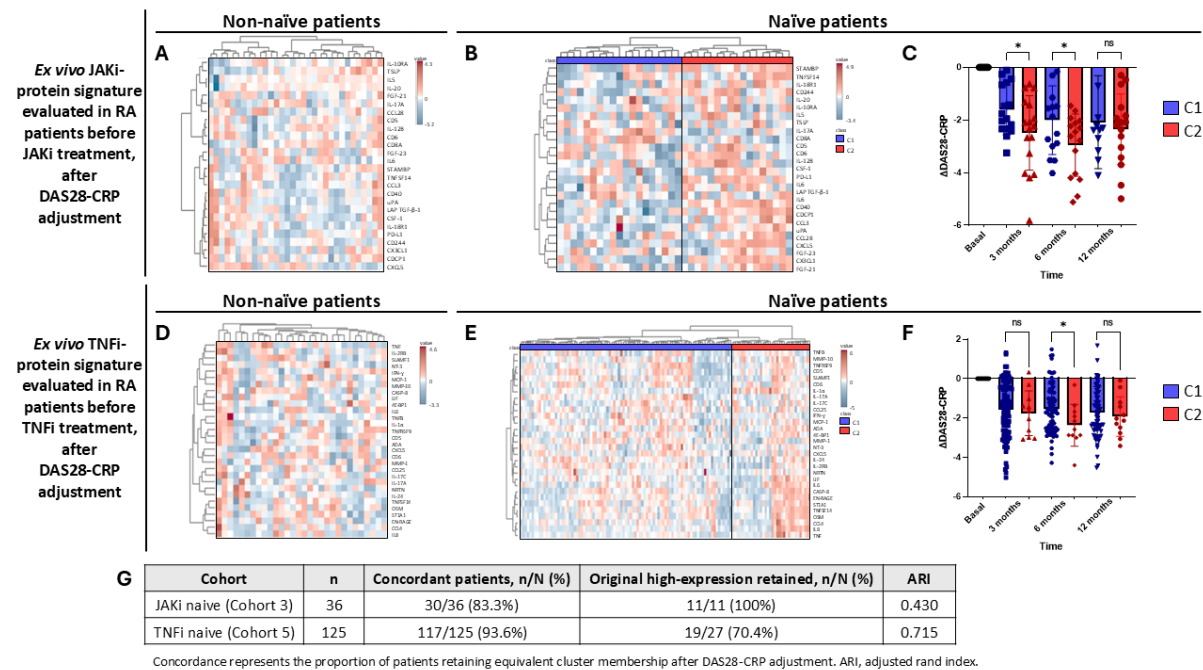




Supplementary Figure S5. Sensitivity analysis of RA patient clustering based on *ex vivo* JAKi- or TNFi-induced protein signatures after adjustment for baseline DAS28-CRP. – (A) Unsupervised clustering heatmap of non-naïve RA patients starting JAKi treatment (Cohort 2), based on the *ex vivo* JAKi-induced protein signature after adjustment for baseline DAS28-CRP, showing no distinct clusters. (B) Same analysis in naïve RA patients initiating JAKi (Cohort 3), showing preservation of two molecular clusters. (C) Clinical response, assessed by Δ DAS28-CRP at 3, 6, and 12 months, according to the adjusted clusters in naïve JAKi-treated patients. (D–E) Equivalent analyses using the *ex vivo* TNFi-induced protein signature in non-naïve (Cohort 4) and naïve (Cohort 5) RA patients after adjustment for baseline DAS28-CRP. No distinct clustering is observed in non-naïve patients (D), whereas two molecular clusters are retained in naïve patients (E). (F) Δ DAS28-CRP at 3, 6, and 12 months according to the adjusted clusters in naïve TNFi-treated patients. (G) Concordance between original and DAS28-CRP-adjusted cluster assignments in naïve patients. ARI, adjusted Rand index.

Statistical significance: * $p < 0.05$, ** $p < 0.01$; ns: not significant.