

Supplementary Table S11. Consistency of the association between treatment-matched molecular clusters and Δ DAS28-CRP across individual agents within the JAKi and TNFi therapeutic classes.

**A. JAKi signature-defined clusters in JAKi-treated b/tsDMARD-naïve RA patients:
baricitinib vs other JAKi**

Time	C1-Baricitinib Δ DAS28-CRP, mean $\pm$ SD	C2-Baricitinib Δ DAS28-CRP, mean $\pm$ SD	C1-Other JAKi Δ DAS28-CRP, mean $\pm$ SD	C2-Other JAKi Δ DAS28-CRP, mean $\pm$ SD	Cluster $\times$ Drug p-value
3 months	-1.87 $\pm$ 1.04	-3.18 $\pm$ 1.65	-1.31 $\pm$ 0.92	-2.39 $\pm$ 1.54	0.824
6 months	-2.00 $\pm$ 1.36	-3.45 $\pm$ 1.28	-2.20 $\pm$ 0.64	-3.25 $\pm$ 1.10	0.727
12 months	-1.85 $\pm$ 1.56	-2.63 $\pm$ 1.46	-2.09 $\pm$ 1.43	-3.16 $\pm$ 1.39	0.834

**B. TNFi signature-defined clusters in TNFi-treated b/tsDMARD-naïve RA patients:
etanercept vs other TNFi**

Time	C1-Etanercept Δ DAS28-CRP, mean $\pm$ SD	C2-Etanercept Δ DAS28-CRP, mean $\pm$ SD	C1-Other TNFi Δ DAS28-CRP, mean $\pm$ SD	C2-Other TNFi Δ DAS28-CRP, mean $\pm$ SD	Cluster $\times$ Drug p-value
3 months	-1.21 $\pm$ 1.33	-1.92 $\pm$ 1.06	-1.59 $\pm$ 1.39	-1.77 $\pm$ 1.31	0.570
6 months	-1.56 $\pm$ 1.53	-2.56 $\pm$ 0.55	-1.70 $\pm$ 1.39	-2.09 $\pm$ 1.35	0.540
12 months	-2.27 $\pm$ 0.83	-1.73 $\pm$ 0.43	-1.59 $\pm$ 1.37	-2.13 $\pm$ 1.14	0.329

Values represent observed changes in DAS28-CRP from baseline and are presented as mean $\pm$ SD. JAKi signature-defined clusters were evaluated in JAKi-treated patients, and TNFi signature-defined clusters in TNFi-treated patients. At each time point (3, 6, and 12 months), an exploratory linear model including molecular cluster, treatment agent group, and the Cluster $\times$ Drug interaction was fitted separately. The interaction p-value assesses whether the association between molecular cluster and Δ DAS28-CRP differs according to the specific agent group within the same therapeutic class. JAKi were categorized as baricitinib *versus* other JAKi (tofacitinib, upadacitinib, and filgotinib), and TNFi as etanercept *versus* other TNFi (adalimumab, infliximab, certolizumab, and golimumab).