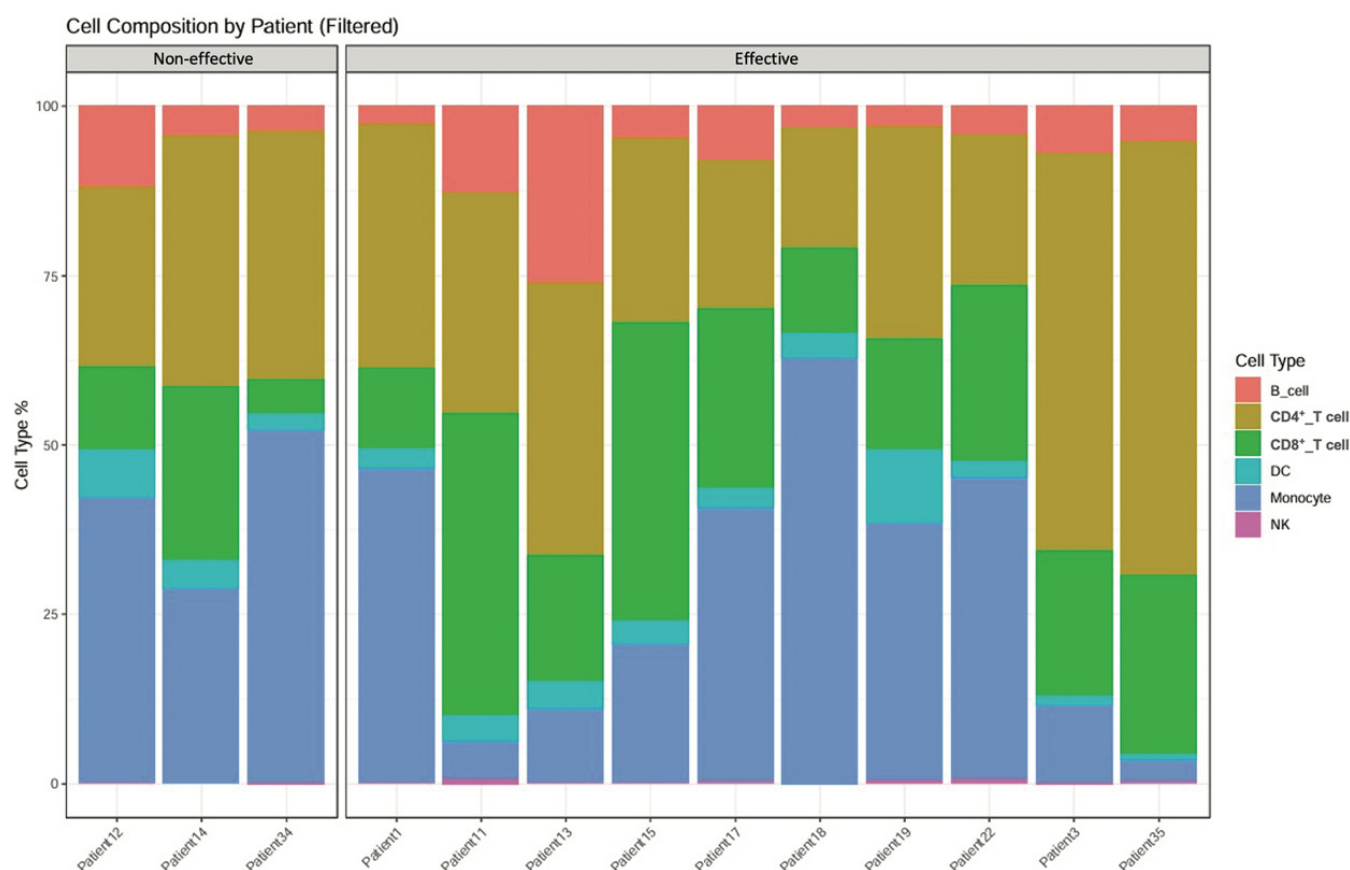




Supplementary Fig. S1. Distinct immune cell compositions associated with JAKi response.

Stacked bars show the relative proportions of major immune cell subsets per patient, stratified by JAK inhibitor response (Non-effective vs. Effective). Colours denote B cells, CD4⁺ T cells, CD8⁺ T cells, dendritic cells (DC), monocytes, and natural killer (NK) cells; each bar sums to 100% (y-axis: percentage). Only cells passing QC and doublet removal were included. Formal group comparisons are provided in the Supplementary file.

Supplementary Table S1. Prespecified candidate genes grouped by mechanism (HGNC symbols).

Group	Related gene	Reference
Related to csDMARDs	<i>MTHFR, ABCB1, ABCC2, FPGS, GGH AMPD, ITPA, and ADA</i>	[17]
Related to immunity and inflammation	<i>HLA-DRB1, ETS1, EZH1, FOXP3, IL2, IL2RA, IL22, IRF4, JAK3, KMT2A, LTK, NFKB1, REL, RELA, TBX21, SATB1, STAT5A, STAT5B, YY1, YBX1, COL1A1, COL3A1, CTLA4, TNF, TRAF</i>	[18, 19]
Related to JAK-STAT pathway	<i>IL6ST, IL6, IRF1, JAK1, JAK2, JAK3, SOCS1, SOCS3, STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B, STAT6, TYK2</i>	[14, 20, 21]
Related to JAKi	<i>IFNGR1, IL10RA, IL12RB1, IL6, JAK1, JAK2, JAK3, SOCS1, SOCS3, STAT1, STAT3, STAT4, STAT5, STAT6, TYK2, CXCL10, CCL2, CCL5, CSF1, FN1, ICAM1, IL1B, IRAK1, MMP3, MMP9, MYD88, NFKB1, PTGS2, RELA, ADAMTS4, ADAMTS5, VCAM1, VEGFA</i>	[22-25]

Gene symbols follow HGNC; categories are mechanism-based (csDMARDs, immunity/inflammation, JAK-STAT, JAK inhibitor-related). Genes may appear in multiple categories. Reference numbers correspond to the main reference list.

Supplementary Table S2. The association of SNPs with the response to JAK inhibitors.

SNPs	RA patients (n=275)				p-value
	Effective (n=217)		Non-effective (n=58)		
	n	%	n	%	
rs1024611	170	78.7	36	63.2	0.015*
rs1045642	124	57.1	36	62.1	0.499
rs1051266	148	68.2	47	81.0	0.056
rs10974944	99	45.6	34	58.6	0.079
rs11258747	26	12.0	6	10.5	0.761
rs1127354	75	34.6	30	52.6	0.013*
rs1128334	118	55.4	34	58.6	0.661
rs1143627	159	73.3	41	70.7	0.695
rs11545077	80	37.0	24	41.4	0.545
rs11545078	37	17.1	11	19.0	0.733
rs12203592	0	0	0	0	-
rs12722489	53	24.4	12	20.7	0.552
rs13031237 †	7	3.2	0	0	0.351
rs1544105	116	53.5	28	48.3	0.483
rs1570360	67	31.3	18	31.6	0.969
rs16944	159	73.3	39	68.4	0.467
rs17602729	0	0	0	0	-
rs1800629	24	11.1	10	17.2	0.204
rs1800795 †	0	0	1	1.7	0.211
rs1800909	80	36.9	24	41.4	0.529
rs2010963	144	66.7	38	65.5	0.869
rs20417 †	16	7.4	6	10.3	0.425
rs2104286	54	24.9	12	20.7	0.506
rs2230624	0	0	0	0	-
rs2240017	52	24.0	12	20.7	0.600
rs2242480	105	48.6	25	43.1	0.456
rs231775	103	47.5	34	59.7	0.102
rs2372536	118	54.4	28	48.3	0.408
rs244076	56	25.8	17	29.3	0.591
rs2740574	0	0	0	0	-
rs281432	96	44.2	23	40.4	0.598
rs2830585	34	15.6	11	19.0	0.546
rs2857657	32	14.8	7	12.1	0.604
rs3087243 †	69	31.8	23	39.7	0.260
rs3212752 †	17	7.8	3	5.2	0.776
rs3212780	6	2.8	4	6.9	0.226
rs3213409	0	0	0	0	-
rs34536443	0	0	0	0	-
rs35037722	38	17.6	9	15.8	0.748
rs35599367	0	0	0	0	-
rs3746444	53	24.4	16	27.6	0.622
rs3758149	80	36.9	24	41.4	0.529
rs4553808	37	17.2	14	25.5	0.163
rs4586	170	78.3	37	63.8	0.023*
rs4750316	42	19.4	11	19.0	0.947
rs4794067	52	24.0	13	22.4	0.805
rs4796793	144	66.4	41	70.7	0.532
rs4937333	141	65.0	39	67.2	0.747
rs5498	89	41.0	26	44.8	0.601
†rs6822844	1	0.5	0	0	1.000
rs699947	102	47	21	36.2	0.142
rs702873	42	19.4	8	13.8	0.329
rs7039789	78	35.9	19	32.8	0.652
rs717620	78	36.3	15	26.3	0.159
rs7270101	0	0	0	0	-
rs744166	151	69.9	41	70.7	0.908
rs7574865	128	59.3	34	58.6	0.930
rs947474	42	19.4	11	19.0	0.947

p-values compare carrier frequencies (heterozygous or homozygous for the effect allele) between the Effective and Non-effective groups using χ^2 or Fisher's exact test. † indicates Fisher's exact test. The significance is indicated as * $p < 0.05$, ** $p < 0.01$

Supplementary Table S3. Clinical and demographic description of 13 RA patients.

Variables	Effective (n=10)		Non-effective (n=3)		<i>p</i> -value
	n	%	n	%	
Age, mean $\pm$ SD (years)	57.4 $\pm$ 10.76		63.67 $\pm$ 7.09		0.290
Sex [†]					0.528
Female	7	70	3	100	
Male	3	30	0	0	
Duration of RA, mean $\pm$ SD (years)	6.9 $\pm$ 7.0		14.3 $\pm$ 7.0		0.139
BMI, mean $\pm$ SD (kg/m ²)	23.2 $\pm$ 2.5		26.35 $\pm$ 6.96		0.336
Smoking [‡]	2	20	0	0	1.000
Alcohol use, n (%)	0	0	0	0	-
Comorbidities, n (%)					
Hypertension [†]	3	30	2	20	0.511
Type 2 diabetes mellitus	0	0	0	0	-
Chronic kidney disease [†]	1	10	1	33.3	0.423
Coronary artery disease	0	0	0	0	-
SNP carriers (heterozygous or homozygous), n (%)					
rs1024611 [†]	3	42.9	2	66.7	1.000
rs1127354 [†]	2	28.6	1	33.3	1.000
rs4586 [‡]	3	42.9	2	66.7	1.000
Lab data					
RF positivity ($\geq$ 30 U/mL), n (%) [†]	7	70	2	66.67	1.000
ACPA positivity ($>$ 10 U/mL), n (%)	4	50	2	100	0.467
DAS28-ESR, mean $\pm$ SD	4.2 $\pm$ 1.5		5.0 $\pm$ 1.5		0.443
CRP (mg/dL), mean $\pm$ SD	2.1 $\pm$ 2.5		3.0 $\pm$ 3.2		0.623
ESR (mm/h), mean $\pm$ SD	33.5 $\pm$ 35.3		83 $\pm$ 48.2		0.073
Concomitant csDMARDs, n (%)					
Methotrexate	10	100	3	100	-
Sulfasalazine [†]	7	70	2	66.7	1.000
Leflunomide [†]	3	30	3	100	0.070
Hydroxychloroquine [†]	10	100	2	66.7	0.231

Mean $\pm$ SD for continuous variables and n (%) for categorical variables. *p*-values were calculated using Student's *t*-test for continuous variables and Fisher's exact test for categorical variables (variables marked with [†]).

BMI: Body Mass Index, ACPA: anti-cyclic citrullinated peptide antibodies; CRP: C-reactive protein; DAS28: Disease Activity Score in 28 joints; ESR: erythrocyte sedimentation rate; RF: rheumatoid factor; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs.