

Supplementary Fig. S1. Flowchart showing inclusion of patients with seropositive RA for the analysis of cancer incidence.

RA: rheumatoid arthritis.

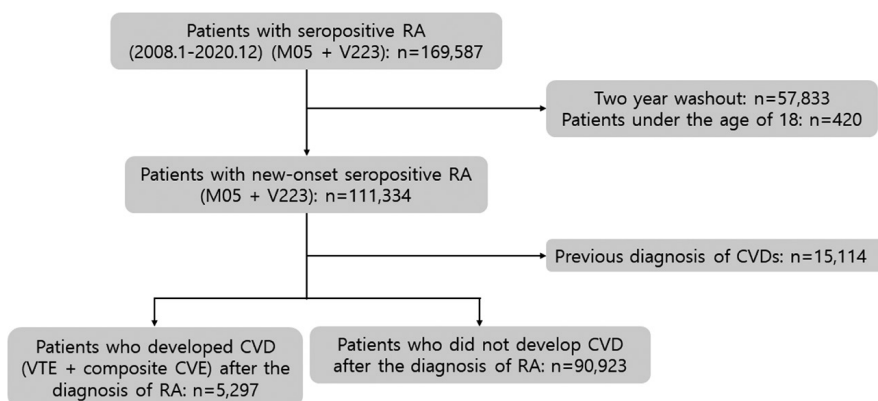
Supplementary Table S1. Comparison of patient characteristics at the time of starting the first JAKi/biologics and analysed for cancer incidence.

	Total (n=10641)	RA patients with cancer (n=378)	RA patients without cancer (n=10263)	p-value
Age at diagnosis, mean \pm SD	49.99 \pm 14.02	59.68 \pm 12.13	49.63 \pm 13.96	<0.001
Age group at diagnosis				
<20	229 (2.2)	0 (0.0)	229 (2.2)	<0.001
20-34	1360 (12.8)	12 (3.2)	1348 (13.1)	
35-49	3290 (30.9)	60 (15.9)	3230 (31.5)	
50-64	4160 (39.1)	168 (44.4)	3992 (38.9)	
≥ 65	1602 (15.0)	138 (36.5)	1464 (14.3)	
Sex, n (%)				
Female	8087 (76.0)	251 (66.4)	7836 (76.4)	<0.001
Male	2554 (24.0)	127 (33.6)	2427 (23.6)	
Type of insurance, n (%)				
National Health Insurance	10082 (94.8)	357 (94.4)	9725 (94.8)	0.880
Medical Aid	559 (5.2)	21 (5.6)	538 (5.2)	
Underlying disease, n (%) [‡]				
Hypertension	2495 (23.5)	155 (41.0)	2340 (22.8)	<0.001
Diabetes mellitus	1673 (15.7)	114 (30.2)	1559 (15.2)	<0.001
Dyslipidaemia	3726 (35.0)	209 (55.3)	3517 (34.3)	<0.001
csDMARD usage [§]				
Methotrexate	6413 (60.3)	323 (85.5)	6090 (59.3)	<0.001
Hydroxychloroquine	5722 (53.8)	190 (50.3)	5532 (53.9)	0.180
Sulfasalazine	2899 (27.2)	125 (33.1)	2774 (27.0)	0.011
Tacrolimus	120 (1.1)	70 (18.5)	50 (0.5)	<0.001
Leflunomide	690 (6.5)	153 (40.5)	537 (5.2)	<0.001

[‡]Medical history within one year prior to initiating JAKi/biologics were assessed.

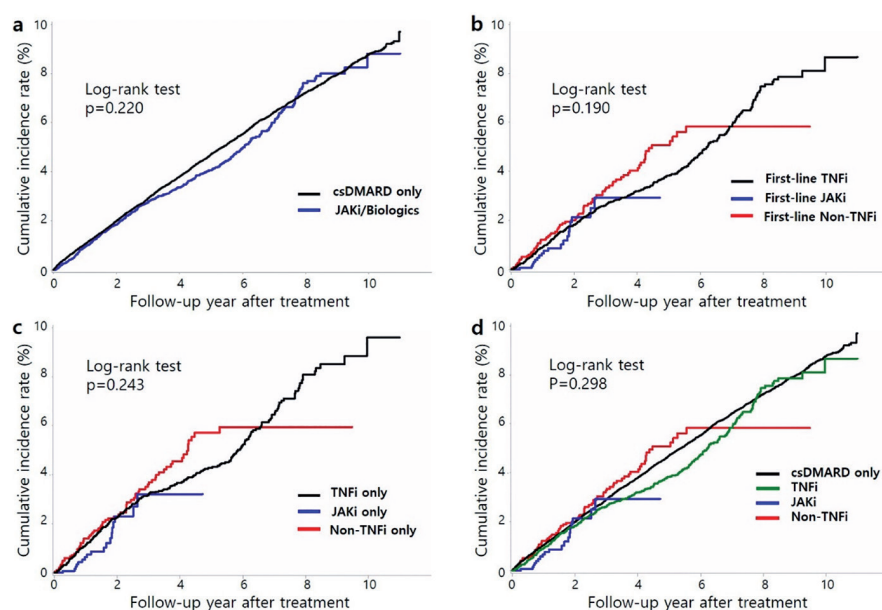
[§]csDMARD usage within six months of initiating the first JAKi/biologics were counted.

JAKi: Janus kinase inhibitor, RA: rheumatoid arthritis, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug.



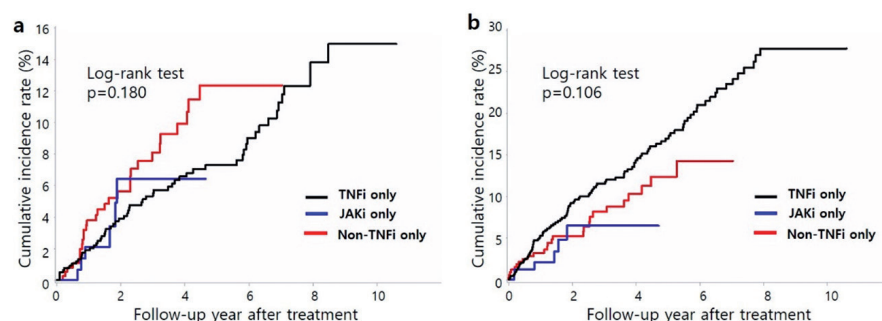
Supplementary Fig. S2. Flowchart illustrating selection of patients with seropositive RA for the analysis of CVDs occurrence.

RA: rheumatoid arthritis, CVD: cardiovascular diseases, VTE: venous thromboembolic events, CVE: cardiovascular events.



Supplementary Fig. S3. Comparison of cumulative incidence of cancers according to patient treatment. The risk of overall cancers was similar in patients that were (a) prescribed with JAKi/biologics and csDMARDs, as well as in (b) those who used JAKi, TNFi, and non-TNFi as the first-line treatment. In addition, there was no difference in the incidence of cancers among (c) those who were treated with only JAKi, TNFi, and non-TNFi during the follow-up and between (d) JAKi, TNFi, non-TNFi, and csDMARDs users.

JAKi: Janus kinase inhibitors, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug, TNFi: tumour necrosis factor- α inhibitor.



Supplementary Fig. S4. Kaplan-Meier analysis comparing cancers and CVDs incidence among JAKi, TNFi, and non-TNFi only users aged ≥ 65 years.

The incidence of (a) cancers and (b) CVDs according to JAKi, TNFi, and non-TNFi usage was comparable in those aged ≥ 65 years.

CVD: cardiovascular diseases, JAKi: Janus kinase inhibitors, TNFi: tumour necrosis factor- α inhibitor.

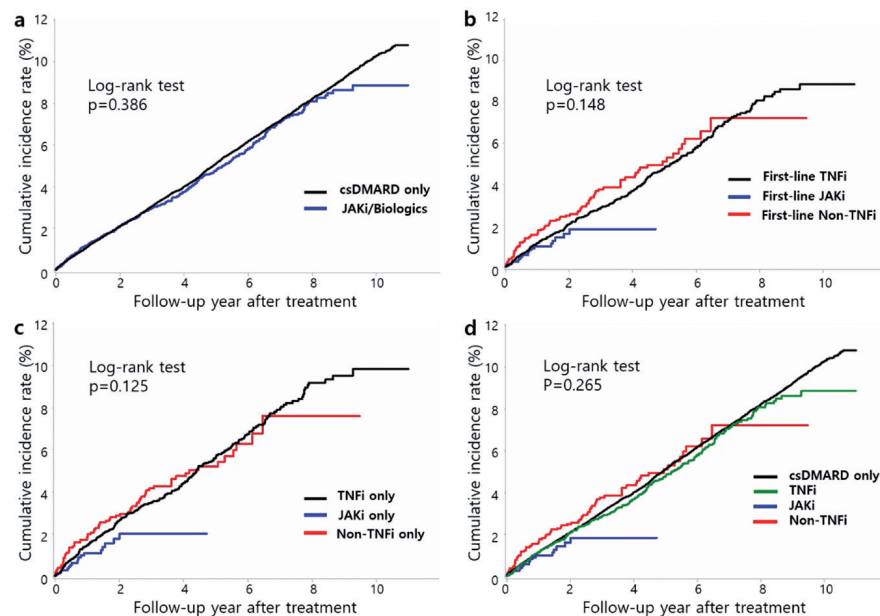
Supplementary Table S2. Patient characteristics at the period of initiating the first JAKi/biologics and analysed for CVDs incidence.

	Total (n=10173)	RA patients with CVD (n= 410)	RA patients without CVD (n=9763)	p-value
Age at diagnosis, mean \pm SD	49.25 \pm 13.87	63.25 \pm 11.25	48.66 \pm 13.66	<0.001
Age group at diagnosis				
<20	230 (2.3)	0 (0.0)	230 (2.4)	<0.001
20-34	1378 (13.5)	7 (1.7)	1371 (14.0)	
35-49	3259 (32.0)	31 (7.6)	3228 (33.1)	
50-64	3956 (38.9)	174 (42.4)	3782 (38.7)	
≥ 65	1350 (13.3)	198 (48.3)	1152 (11.8)	
Sex, n (%)				
Female	7812 (76.8)	270 (65.9)	7542 (77.3)	<0.001
Male	2361 (23.2)	140 (34.1)	2221 (22.7)	
Type of insurance, n (%)				
National Health Insurance	9649 (94.9)	379 (92.4)	9270 (95.0)	0.032
Medical Aid	524 (5.1)	31 (7.6)	493 (5.0)	
Underlying disease, n (%) [‡]				
Hypertension	2130 (20.9)	226 (55.1)	1904 (19.5)	<0.001
Diabetes mellitus	1485 (14.6)	158 (38.5)	1327 (13.6)	<0.001
Dyslipidaemia	3424 (33.7)	241 (58.8)	3183 (32.6)	<0.001
csDMARD usage [§]				
Methotrexate	6234 (61.3)	345 (84.2)	5889 (60.3)	<0.001
Hydroxychloroquine	5532 (54.4)	196 (47.8)	5336 (54.7)	0.007
Sulfasalazine	2788 (27.4)	145 (35.4)	2643 (27.1)	<0.001
Tacrolimus	148 (1.5)	97 (23.7)	51 (0.5)	<0.001
Leflunomide	698 (6.9)	182 (44.4)	516 (5.3)	<0.001

[‡]Medical history within one year prior to initiating JAKi/biologics were assessed.

[§]csDMARD usage within six months of initiating the first JAKi/biologics were counted.

JAKi: Janus kinase inhibitor, CVD: cardiovascular disease, RA: rheumatoid arthritis, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug.

**Supplementary Fig. S5.** Cumulative incidence of CVDs according to medication prescription.

The cumulative incidence of overall CVDs was comparable among patients who were (a) treated with JAKi/biologics and csDMARDs and in (b) patients who were prescribed JAKi, TNFi, and non-TNFi as a first-line therapeutic agent. Meanwhile, the occurrence of CVDs was also similar in (c) patients who used JAKi, TNFi, and non-TNFi only during the observation period, and in those treated with (d) JAKi, TNFi, and non-TNFi, and csDMARDs only.

CVD: cardiovascular diseases, JAKi: Janus kinase inhibitors, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug, TNFi: tumour necrosis factor- α inhibitor.