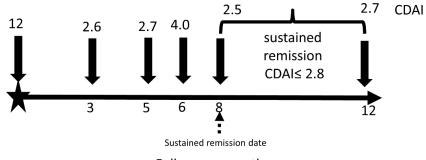
ACPA and RF, and sustained clinical remission - May 9, 2018

Supplementary Information

Figure S1: Example of sustained remission definition



Follow-up, months

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Table S1: Association between ACPA/RF status at baseline and CDAI over time using GLMMs

	Regression coefficients (standard error), <i>p-value</i>			
	Unadjusted model	Adjusted models		
		Model 1	Model 2	Model 3
ACPA status at baseline				
- ACPA neg/RF neg	Ref	Ref	Ref	Ref
- ACPA neg /RF pos	-1.19 (1.01), 0.24	0.48 (0.73), 0.51	0.51 (0.71), 0.47	0.95 (0.75), 0.20
- ACPA pos /RF neg	-2.96 (1.29), 0.02	-0.63 (0.94), 0.50	-0.73 (0.90), 0.42	-0.59 (0.96), 0.54
- ACPA pos /RF pos	-2.73 (0.69), <0.0001	-1.63 (0.50), 0.001	-1.41 (0.49), 0.004	-1.39 (0.51), 0.01
Time (month)	-0.15 (0.01), <0.0001	-0.15 (0.004), <0.0001	-0.15 (0.004), <0.0001	-0.13 (0.004), <0.0001
Female	0.73 (0.70), 0.30	1.91 (0.51), 0.0002	1.57 (0.50), 0.002	1.64 (0.52), 0.002
Age at baseline	-0.02 (0.02), 0.34	-0.02 (0.02), 0.23	-0.07 (0.02), <0.0001	-0.09 (0.02), <0.0001
CDAI at baseline	0.43 (0.02)	0.43 (0.02), <0.0001	0.42 (0.02), <0.0001	0.42 (0.02), <0.0001
Number of comorbidities at baseline	0.67 (0.11), <0.0001	-	0.70 (0.09), <0.0001	0.74 (0.10), <0.0001
Use of csDMARDs over time	0.37 (0.23), 0.11	-	-	-
Number of csDMARDs over time	0.84 (0.14), <0.0001	-	-	-0.33 (0.13), 0.01

Model 1: adjusted for age, sex, time, and CDAI at baseline

ACPA: anti-citrullinated protein antibody; RF: rheumatoid factor; CDAI: clinical disease activity index; bDMARDs: biologic disease modifying antirheumatic drugs; csDMARDs: conventional synthetic disease modifying antirheumatic drugs

Model 2: adjusted for age, sex, time, CDAI at baseline, number of comorbidities at baseline,

Model 3: adjusted for age, sex, time, CDAI at baseline, number of comorbidities at baseline, and number of csDMARDs, use of bDMARDs, and use of oral steroids over time

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Table S2: Association between ACPA/RF status at baseline and SDAI over time using GLMMs

	Regression coefficients (standard error), p-value			
	Unadjusted model	Adjusted models		
		Model 1	Model 2	Model 3
Anti-CCP status at baseline				
 Anti-CCP ^{neg}/RF ^{neg} 	Ref	Ref	Ref	Ref
 Anti-CCP ^{neg} /RF ^{pos} 	-1.41 (1.09), 0.20	0.42 (0.82), 0.61	0.35 (0.80), 0.66	0.97 (0.83), 0.25
 Anti-CCP pos /RF neg 	-3.09 (1.39), 0.03	-0.42 (1.09), 0.70	-0.49 (1.05), 0.64	-0.36 (1.10), 0.74
- Anti-CCP pos /RF pos	-2.57 (0.74), 0.001	-1.45 (0.56), 0.01	-1.20 (0.55), 0.03	-1.16 (0.57), 0.04
Time (month)	-0.15 (0.003), <0.0001	-0.16 (0.004), <0.0001	-0.16 (0.004), <0.0001	-0.15 (0.004), <0.0001
Female at baseline	0.42 (0.76), 0.58	1.82 (0.59), 0.002	1.46 (0.60), 0.06	1.51 (0.59), 0.01
Age at baseline	-0.01 (0.02), 0.57	-0.03 (0.02), 0.11	-0.09 (0.02), <0.0001	-0.10 (0.02), <0.0001
SDAI at baseline	0.43 (0.02), <0.0001	0.43 (0.02), <0.0001	0.43 (0.02), <0.0001	0.43 (0.02), <0.0001
Number of comorbidities at baseline	0.72 (0.12), <0.0001	-	0.72 (0.12), <0.0001	0.82 (0.11), <0.0001
Use of csDMARDs over time	0.13 (0.24), 0.59	-	-	-
Number of csDMARDs over time	0.78 (0.14), <0.0001	-	-	-0.47 (0.14), 0.001
Use of bDMARDs over time	-6.37 (0.24), <0.0001	-	-	-4.32 (0.24), <0.0001
Use of oral steroids over time	2.91 (0.30), <0.0001	-	-	2.86 (0.28), <0.0001

Model 1: adjusted for age, sex, time, and SDAI at baseline

Model 2: adjusted for age, sex, time, SDAI at baseline, and number of comorbidities at baseline

Model 3: adjusted for age, sex, time, SDAI at baseline, and number of comorbidities at baseline, number of csDMARDs, use of bDMARDs, and use of oral steroids over time

ACPA: anti-citrullinated protein antibody; RF: rheumatoid factor; SDAI: simplified disease activity score; bDMARDs: biologic disease modifying antirheumatic drugs; csDMARDs: conventional synthetic disease modifying antirheumatic drugs

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Table S3: Association between ACPA/RF status at baseline and DAS28-ESR over time using GLMMs

	Regression coefficients (standard error), p-value			
	Unadjusted model	Adjusted models		
		Model 1	Model 2	Model 3
Anti-CCP status at baseline				
 Anti-CCP ^{neg}/RF ^{neg} 	Ref	Ref	Ref	Ref
 Anti-CCP ^{neg} /RF ^{pos} 	0.04 (0.14), 0.79	0.18 (0.10), 0.08	0.17 (0.10), 0.08	0.25 (0.10), 0.01
 Anti-CCP pos /RF neg 	-0.39 (0.18), 0.03	-0.11 (0.13), 0.39	-0.13 (0.13), 0.31	-0.10 (0.13), 0.50
- Anti-CCP pos /RF pos	-0.10 (0.09), 0.31	-0.02 (0.07), 0.77	0.01 (0.07), 0.92	0.03 (0.07), 0.70
Time (month)	-0.02 (0.0), <0.0001	-0.02 (0.0), <0.0001	-0.02 (0.0), <0.0001	-0.02 (0.001), <0.0001
Female	0.24 (0.10), 0.01	0.29 (0.07), <0.0001	0.25 (0.07), 0.003	0.24 (0.07), 0.001
Age at baseline	0.004 (0.003), 0.14	0.001 (0.002), 0.80	-0.01 (0.002), 0.01	-0.01 (0.003), 0.0002
DAS28-ESR at baseline	0.49 (0.02), <0.0001	0.49 (0.02), <0.0001	0.48 (0.02), <0.0001	0.46 (0.02), <0.0001
Number of comorbidities at baseline	0.11 (0.02), <0.0001	-	0.09 (0.01), 0.0001	0.10 (0.01), <0.0001
Use of csDMARDs over time	0.02 (0.03), 0.47	-	-	-
Number of csDMARDs over time	0.08 (0.02), <0.0001	-	-	-0.09 (0.02), 0.001
Use of bDMARDs over time	-0.85 (0.03), <0.0001	-	-	-0.61 (0.03), <0.0001
Use of oral steroids over time	0.39 (0.04), <0.0001	-	-	0.38 (0.03), <0.0001

Model 1: adjusted for age, sex, time, DAS28-ESR at baseline

Model 2: adjusted for age, sex, time, DAS28-ESR at baseline, and number of comorbidities at baseline

Model 3: adjusted for age, sex, time, DAS28-ESR at baseline, number of comorbidities at baseline, and number of csDMARDs, use of

 $\ensuremath{\mathsf{bDMARDs}}\xspace$, and use of oral steroids over time

ACPA: anti-citrullinated protein antibody; RF: rheumatoid factor; DAS28-ESR: 28-joint disease activity score; bDMARDs: biologic disease modifying antirheumatic drugs; csDMARDs: conventional synthetic disease modifying antirheumatic drugs

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Table S4: Association between ACPA status at baseline and time to first sustained remission using Cox proportional hazards regression analysis

	Hazard Ratio (95% Confidence Interval), <i>p-value</i>				
	Unadjusted model	Adjusted models			
		Model 1	Model 2	Model 3	
ACPA at baseline¥					
- ACPA neg	Ref	Ref	Ref	Ref	
- ACPA pos	1.45 (1.15-1.82), 0.002	1.43 (1.08-1.89), 0.01	1.41 (1.06-1.88), 0.02	1.37 (1.03-1.81), 0.03	
RF status at baseline [¥]					
- RF ^{neg}	Ref	Ref	Ref	Ref	
- RF ^{pos}	1.20 (0.95-1.52), 0.12	0.93 (0.70-1.24), 0.62	0.88 (0.66-1.18), 0.38	0.88 (0.66-1.17), 0.36	
Female	0.96 (0.74-1.23), 0.73	0.79 (0.61-1.02), 0.07	0.85 (0.65-1.10), 0.20	0.85 (0.66-1.11), 0.24	
Age at baseline	0.99 (0.98-1.00), 0.02	0.99 (0.99-1.01), 0.18	1.00 (0.99-1.01), 0.56	1.00 (0.99-1.01), 0.57	
CDAI at baseline	0.97 (0.96-0.98), <0.0001	0.98 (0.97-0.99), <0.0001	0.98 (0.97-0.99), 0.0001	0.99 (0.98-0.99), 0.002	
Number of comorbidities at baseline	0.87 (0.83-0.91), <0.0001	-	0.89 (0.84-0.93), <0.0001	0.90 (0.85-0.94), <0.0001	
Use of csDMARDs over time	2.85 (1.88-4.34), <0.0001	-	-	2.84 (1.73-4.69), <0.0001	
Number of csDMARDs over time	1.24 (1.11-1.40), 0.0003	-	-	0.97 (0.83-1.13), 0.69	
Use of oral steroids over time	0.58 (0.41-0.82), 0.002	-	-	0.64 (0.45-0.91), 0.01	

Model 1: adjusted for age, sex, RF status, and CDAI at baseline

Model 2: adjusted for age, sex, rheumatoid factor, CDAI at baseline, and number of comorbidities at baseline

Model 3: adjusted for age, sex, rheumatoid factor, CDAI at baseline, and number of comorbidities at baseline, use of csDMARDs, number of csDMARDs and use of oral steroids over time

ACPA: anti-citrullinated protein antibody; RF: rheumatoid factor; CDAI: clinical disease activity index; bDMARDs: biologic disease modifying antirheumatic drugs; csDMARDs: conventional synthetic disease modifying antirheumatic drugs

 $^{^{}f Y}$ Interaction between ACPA and RF in all models were checked and it was not significant

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Table S5: Association between ACPA status at baseline and CDAI over time

	Regression coefficients (standard error), p-value				
	Unadjusted model	Adjusted models			
		Model 1	Model 2	Model 3	
ACPA status at baseline¥					
- ACPA ^{neg}	Ref	Ref	Ref	Ref	
- ACPA pos	-2.38 (0.60), <0.0001	-1.61 (1.48), 0.003	-1.51 (0.53), 0.004	-1.75 (0.56), 0.002	
Time (month)	-0.18 (0.01), <0.0001	-0.15 (0.004), <0.0001	-0.15 (0.003), <0.0001	-0.13 (0.004), <0.0001	
RF status at baseline [¥]					
- RF ^{neg}	Ref	Ref	Ref	Ref	
- RF ^{pos}	-1.88 (0.62), 0.003	-0.12 (0.56), 0.83	0.02 (0.54), 0.97	0.24 (0.58), 0.68	
Female at baseline	0.73 (0.70), 0.30	1.90 (0.51), 0.0002	1.56 (0.50), 0.002	1.63 (0.53), 0.002	
Age at baseline	-0.01 (0.02), 0.66	-0.02 (0.02), 0.24	-0.07 (0.02), <0.0001	-0.09 (0.02), <0.0001	
CDAI at baseline	0.43 (0.02), <0.0001	0.43 (0.02), <0.0001	0.42 (0.02), <0.0001	0.41 (0.02),<0.0001	
Number of comorbidity at baseline	0.58 (0.17), 0.001	-	0.71 (0.09), <0.0001	0.74 (0.09), <0.0001	
Use of csDMARDs over time	0.02 (0.33), 0.94	-	-	-	
Number of csDMARDs over time	0.40 (0.19), 0.03	-	-	-0.33 (0.13), 0.001	
Use of bDMARDs over time	-7.36 (0.35), <0.0001	-	-	-4.25 (0.22), <0.0001	
Use of oral steroids over time	4.16 (0.42), <0.0001	-	-	2.74 (0.26), <0.0001	

Model 1: adjusted for age, sex, RF status, time, and CDAI at baseline

Model 2: adjusted for age, sex, time, RF status, CDAI at baseline, and number of comorbidities at baseline

Model 3: adjusted for age, sex, time, RF status, CDAI at baseline, number of comorbidities at baseline, and number of csDMARDs, use of

bDMARDs, and use of oral steroids over time

Fonts in bold show *p-value* < 0.05

 $^{^{\}mbox{\ensuremath{\mathfrak{Y}}}}$ Interaction between ACPA and RF in all models was checked and it was not significant