

Supplemental Figure 1: Out of the sample of patients from the SERA cohort who had AMPA measured (n=396), 233 patients with RA had suitable radiographs after scoring by the modified Sharp-van der Heijde method.

	All RA patients	RA patients with radiographs	P value All RA patients vs RA patients with radiographs
	n=362	n=233	
Demographics			
Female, no. (%)	244 (67.4)	153 (65.7)	0.67 [§]
Age, mean ± SD years	58.2 ± 13.4	58.1 ± 13.3	0.88
Never Smoked, no. (%)	134 (37.0)	85 (36.5)	0.90 [§]
Baseline Characteristics			
Disease duration, mean ± SD months months	14.4 ± 31.1	13.2 ± 24.9	0.97
Swollen joints (0–28), mean ± SD years	7.1 ± 5.1	6.8 ± 5.0	0.42
Tender joints (0– 28), mean ± SD years	9.4 ± 7.0	10.2 ± 7.2	0.22
ESR, mean ± SD mm/hour (complete data)	32.3 ± 25.0 (303)	31.6 ± 23.8 (198)	0.88
CRP, mean ± SD mg/liter (complete data)	24.8 ± 32.6 (331)	24.2± 33.8 (204)	0.66
HAQ DI score (0– 3), mean ± SD (complete data)	1.2 ± 0.8 (361)	1.2 ± 0.8 (232)	0.51
HAD score (0-21), mean ± SD (complete data)	12.1 ± 7.8 (355)	12.3± 7.7 (230)	0.82
EQ5D index value, mean ± SD (complete data)	0.48 ± 0.32 (361)	0.49 ± 0.33 (232)	0.84
DASVAS (0- 100mm) mean ± SD	50.4 ± 26.1	48.9 ± 25.9	0.44
IgM RF high positive, no. (%)	141 (39.0)	86 (36.9)	
IgM RF low	61 (16.9)	42 (18.0)	

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positive, no. (%)			
IgM RF negative,	160 (44.2)	105 (45.1)	0.86 [§]
no. (%)			
CCP high positive,	247 (68.2)	167 (71.7)	
no. (%)			
CCP low positive,	37 (10.2)	18 (7.7)	
no. (%)			
CCP negative, no.	78 (21.5)	48 (20.6)	0.53 [§]
(%)	, ,	, ,	
Baseline Disease			
Activity			
1300330			
DAS28-ESR (0-	5.1 ± 1.3	5.1 ± 1.4 (198)	0.87
9.4), mean ± SD	(303)	0.1 - 1. (130)	
(complete data)	(303)		
DAS28-CRP (0–	4.7 ± 1.6	4.7 ± 1.6 (204)	0.98
9.4), mean ± SD	(331)	4.7 ± 1.0 (204)	0.30
	(221)		
(complete data)			
Change in disease			
activity over one			
year			
DAS28ESR delta	-1.6 ± 1.6	-1.6 ± 1.5 (181)	0.75
mean ± SD	(266)		
(complete data)			
DAS28CRP delta	-2.2 ± 1.9	-2.2 ± 1.8 (152)	0.81
mean ± SD	(241)		
(complete data)			
EULAR response			
over one year			
using DAS28ESR			
Complete Data	266	181	
Good (percentage	104 (39.1)	69 (38.1)	
within group)			
Moderate	83 (31.2)	58 (32.0)	
(percentage	55 (52.2)		
within group)			
No Response	79 (29.7)	54 (29.8)	0.97 [§]
(percentage	13 (23.7)	J T (23.0)	0.57
within group)	 	nahing for all mationts with	RA who had antibodies to PTM

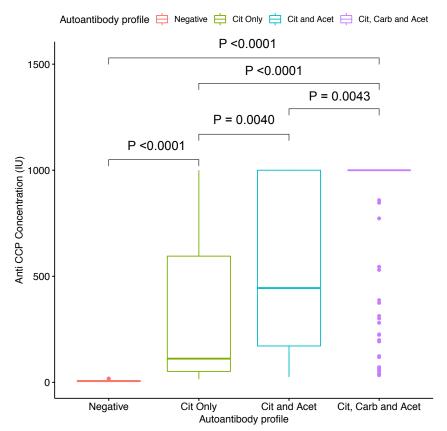
Supplemental Table 1: Baseline Demographics for all patients with RA who had antibodies to PTM measured (n=362) and those patients with RA and radiographs suitable for analysis (n=233). Mann-Whitney-Wilcoxon U test was calculated for each row and p value between All RA patients and RA patients with radiographs is shown in the right hand column. § denotes Egon Pearson N-1 corrected Chi-Squared test for proportions. Significant values of P < 0.05 are denoted in bold.

Comparison	Estimated mean	Asymptotic	Asymptotic
	difference	lower 95% CI	upper 95% CI
Difference in Total SvH change between baseline and 12 months			
Cit, Carb and Acet: Female v Male	0.3	-1.07	1.69
Cit: Female v Male	0.0	-0.46	0.51
Negative: Female v Male	0.1	-0.58	0.70
Difference in Erosion Score change between baseline and 12 months			
Cit, Carb and Acet: Female v Male	0.5	-0·58	1.66
Cit: Female v Male	0.1	-0.24	0.35
Negative: Female v Male	0.1	-0.37	0.51
Difference in Joint Space Narrowing Score change between baseline and 12 months			
Cit, Carb and Acet: Female v Male	-0.3	-1.21	0.67
Cit: Female v Male	-0.1	-0.57	0.32
Negative: Female v Male	-0.1	-0.49	0.29

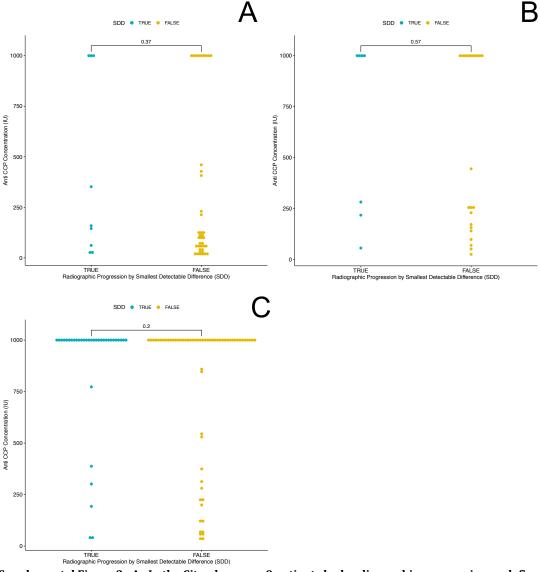
Supplemental Table 2 Estimated mean differences in radiographic progression scores for Female and Male patients summarised by triple positive patients (Cit, Carb and Acet), single positive patients (Cit Only) and autoantibody negative.

	Negative	Cit Only	Cit and Acet	Cit, Carb and Acet	P value Cit, Carb and Acet
		Oy	Acct	una Acct	vs Cit only
	n=47	n=48	n=29	n=97	,
Haemoglobin,	12.9 ± 1.4	13.4 ±	12.7 ±	13.5 ± 1.4	0.59
mean ± SD g/dl	(46)	1.1 (46)	1.8 (29)	(94)	
(complete data)					
Total white cell	8.4 ± 2.3	8.7 ±	8.5 ± 2.8	8.5 ± 2.2	0.72
count, mean ± SD	(46)	2.4 (46)	(29)	(95)	
1x10 ⁶ /dl					
(complete data)					
Neutrophil count,	5.7 ± 2.0	5.7 ±	5.8 ± 2.3	5.6 ± 1.9	0.66
mean ± SD	(46)	1.6 (47)	(29)	(94)	
1x10 ⁶ /dl					
(complete data)					
Lymphocyte	1.8 ± 0.7	2.0 ±	1.8 ± 0.6	1.9 ± 0.6	0.68
count, mean ± SD	(46)	1.0 (47)	(29)	(94)	
1x10 ⁶ /dl					
(complete data)					
Monocyte count,	0.6 ± 0.2	0.6 ±	0.6 ± 0.3	0.6 ± 0.2	0.64
mean ± SD	(46)	0.2 (47)	(29)	(94)	
1x10 ⁶ /dl					
(complete data)	02.01	0.2.1	02101	02.02	0.22
Eosinophil count, mean ± SD	0.2 ± 0.1	0.2 ±	0.2 ± 0.1	0.2 ± 0.2	0.33
1x10 ⁶ /dl	(46)	0.2 (47)	(29)	(94)	
(complete data)					
Platelet count,	363 ± 122	314 ±	375 ±	331 ± 107	0.64
mean ± SD	(46)	64 (47)	123 (29)	(94)	0.04
1x10 ⁶ /dl	(40)	04 (47)	123 (23)	(34)	
(complete data)					
Urea, mean ± SD	6.2 ± 2.3	5.5 ±	7.8 ±	5.5 ± 1.7	0.83
(complete data)	(46)	1.8 (46)	10.2 (28)	(92)	
Creatinine, mean	68.8 ±	64.8 ±	65.4 ±	64.4 ± 13.4	0.95
± SD (complete	13.9 (46)	13.5	17.7 (28)	(93)	
data)		(47)			
Total cholesterol,	5.0 ± 0.8	5.5 ±	4.7 ± 0.8	5.2 ± 1.3	0.11
mean ± SD	(27)	0.9 (32)	(16)	(60)	
(complete data)					
HDL cholesterol,	1.3 ± 0.4	1.4 ±	1.7 ± 0.8	1.3 ± 0.9	0.15
mean ± SD	(25)	0.7 (30)	(15)	(53)	
(complete data)					

Supplemental Table 3: Baseline laboratory tests in patients with RA and radiographs according to anti-PTM antibody status. Mann-Whitney-Wilcoxon U test was calculated for each row and p value between Cit only and Cit, Carb and Acet group is shown in the right hand column.



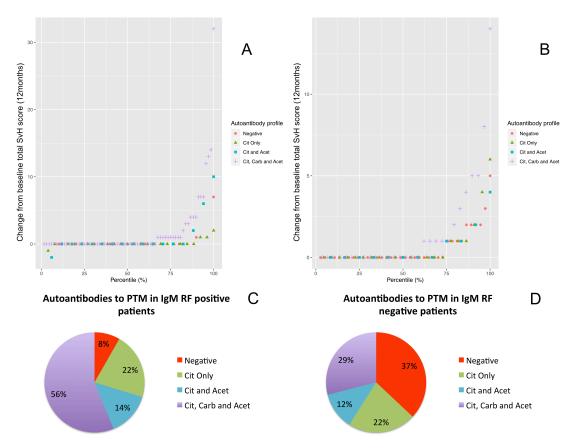
Supplemental Figure 2: In 233 patients with RA and radiographs available for analysis, anti CCP antibody concentration is increased in samples from patients with Cit, Carb and Acet antibodies (n=97) compared to Cit Only (n=48) (1000 IU vs 112 IU, fdr adjusted p value <0.0001). There are also significant differences in anti CCP antibody concentration between the Cit, Carb and Acet group (n=97) and the Cit and Acet group (n=29) (1000 IU vs 445 IU, fdr adjusted p value = 0.0043) and also the Cit and Acet (n=29) and Cit Only group (n=48) (445 IU vs 112 IU, fdr adjusted p value = 0.0040).



Supplemental Figure 3: A: In the Cit only group, 9 patients had radiographic progression as defined by SDD and 39 patients did not. Anti CCP concentration is not statistically different between the patients with radiographic progression and those who do not in this subgroup (Wilcoxon, p=0.37). B: In the Cit and Acet group, 7 patients had radiographic progression as defined by SDD and 22 patients did not. Anti CCP concentration is not statistically different between the patients with radiographic progression and those who do not in this subgroup (Wilcoxon, p=0.57). C: In the Cit, Carb and Acet group, 35 patients had radiographic progression as defined by SDD and 62 did not. Anti CCP concentration is not statistically different between the patients with radiographic progression and those who do not in this subgroup (Wilcoxon, p=0.2).

	Negative	Cit only	Cit and Acet	Cit, Carb and Acet
IgM rheumatoid factor positive (n=121) no. (%)	10 (8.3)	26 (21.5)	17 (14.0)	68 (56.2)
IgM rheumatoid factor negative (n=100) no. (%)	37 (37)	22 (22)	12 (12)	29 (29)

Supplemental Table 4. IgM rheumatoid factor was measured by ELISA from the serum of RA patients with a cut off of 20IU to determine antibody positivity.



Supplemental Figure 4A: IgM RF positive patients with RA and autoantibodies to citrullinated, carbamylated and acetylated proteins (n=68) have higher SVH progression over one year compared to those who have autoantibodies to citrullinated proteins along (n=26) (estimated mean difference $1\cdot2$ 95% CI $0\cdot16-2\cdot21$). There is no statistical difference betweent Cit, Carb and Acet patients (n=68) and Negative patients (n=10) or between Cit, Carb and Acet (n=68) and Cit only patients (n=26). **B:** In IgM RF negative patients, no statistically signficant differences were found when comparing SvH progression over one year in the subgroups Cit, Carb and Acet vs Cit only and Cit only vs Negative. **C:** The proportion of patients in each autoantobody grouping within RA patients who are positive for IgM RF. **D:** The proportion of patients in each autoantobody grouping within RA patients who are negative for IgM RF.

Comparison	Estimated mean	Asymptotic	Asymptotic	
	difference	lower 95% CI	upper 95% CI	
IgM Rheumatoid Factor Positive (n=121)				
Difference in Total SvH change between baseline and 12 months				
	1.2	0.46	2.24	
Cit, Carb and Acet vs Cit Only	1.2	0.16	2.21	
Cit, Carb and Acet vs Negative Cit Only vs Negative	1·0 -0·2	-0·11 -1·05	2·08 0·64	
Difference in Erosion Score change between baseline and 12 months				
Cit, Carb and Acet vs Cit Only	0.9	0.08	1.72	
Cit, Carb and Acet vs Negative	0.9	-0.01	1.65	
Cit Only vs Negative	-0.1	-0.63	0.46	
Difference in Joint Space Narrowing Score change between baseline and 12 months				
C'I Cada ad Assis a C'I Oal	0.6	0.40	1.40	
Cit, Carb and Acet vs Cit Only	0.6	-0.19	1.40	
Cit, Carb and Acet vs Negative Cit Only vs Negative	0·5 -0·1	-0·22 -0·69	1·23 0·48	
Cit Offiny vs (vegative	01	0 03	0 40	
IgM Rheumatoid Factor Negative (n=100)				
Difference in Total SvH change between baseline and 12 months				
Cit, Carb and Acet vs Cit Only	1.3	-0.25	2.79	
Cit, Carb and Acet vs Negative	1.1	-0.49	2.59	
Cit Only vs Negative	-0.2	-1.15	0.71	
Difference in Erosion Score change between baseline and 12 months				

Cit, Carb and Acet vs Cit Only	0.8	-0.25	1.83
Cit, Carb and Acet vs Negative	0.7	-0.34	1.78
Cit Only vs Negative	-0.1	-0.49	0.35
Difference in Joint Space			
Narrowing Score change			
between baseline and 12			
months			
Cit, Carb and Acet vs Cit Only	0.6	-0.43	1.65
Cit, Carb and Acet vs Negative	0.5	-0.41	1.50
Cit Only vs Negative	-0.1	-0.71	0.58

Supplemental Table 5 Estimated mean differences in radiographic progression scores for triple positive patients (Cit, Carb and Acet), single positive patients (Cit Only) and autoantibody negative patients summarised by RF IgM positive and negative status

Comparison	Estimated mean	Asymptotic	Asymptotic
	difference	lower 95% CI	upper 95% CI
Difference in Total Cult shange			
Difference in Total SvH change between baseline and 12			
months			
Cit, Carb and Acet: IgM RF	-0.2	-1.69	1.36
positive v IgM RF negative			
Cit: IgM RF positive v IgM RF negative	-0.1	-0·58	0.43
Negative: IgM RF positive v IgM RF negative	-0.1	-0.76	0.56
THE HEGALIVE			
Difference in Erosion Score			
change between baseline and			
12 months			
Cit Coulo and Appt. IGNA DE	0.2	-1.09	1 42
Cit, Carb and Acet: IgM RF positive v IgM RF negative	0.2	-1.09	1.42
Cit: IgM RF positive v IgM RF	0.0	-0.22	0.32
negative	0.1	0.22	0.45
Negative: IgM RF positive v IgM RF negative	0.1	-0.32	0.45
Difference in Joint Space			
Narrowing Score change			
between baseline and 12			
months			
Cit, Carb and Acet: IgM RF	0.0	-1.13	1.03
positive v IgM RF negative		113	1 03
Cit: IgM RF positive v IgM RF	0.0	-0.46	0.37
negative			
Negative: IgM RF positive v IgM	0.0	-0.49	0.48
RF negative	11.00	<u> </u>	

Supplemental Table 6 Estimated mean differences in radiographic progression scores for RF positive patients and RF negative patients summarised by triple positive patients (Cit, Carb and Acet), single positive patients (Cit Only) and autoantibody negative.