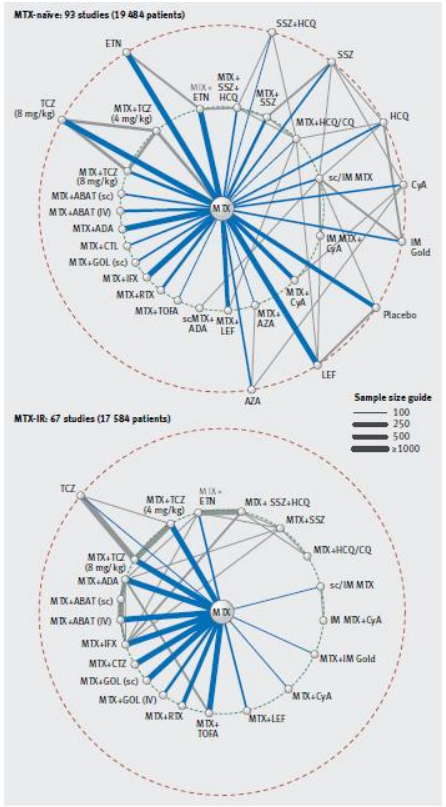
Actualité dans les rhumatismes inflammatoires en 2016?

Alain Saraux

CHU Brest



Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying antirheumatic drugs for rheumatoid arthritis: abridged Cochrane systematic review and network meta-analysis

Glen S Hazlewood,[1, 2, 3, 4] Cheryl Barnabe,[1, 2, 4] George Tomlinson,[5] Deborah Marshall,[2, 4] Dan Devoe,[4] Claire Bombardier[5, 6, 7]

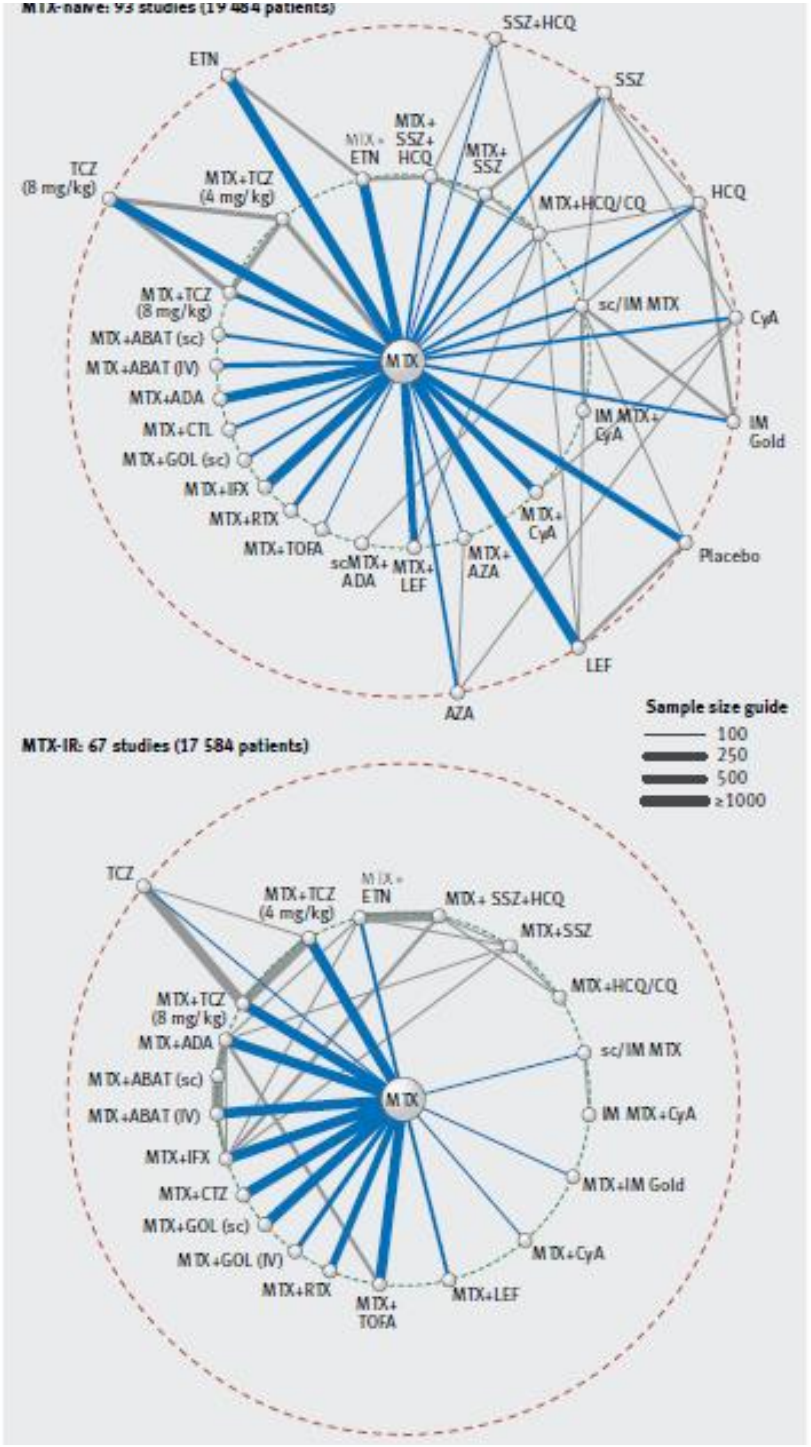


Table 2 | Summary of findings: methotrexate naive patients

Intervention	Absolute risk (95% CrI)	Average treatment effect relative to oral MTX (95% CrI)	Probability treatment superior to oral MTX	No of trials providing direct evidence	Quality of evidence
ACR50 (29 studies; 10 697 patients)	**No of events/1000 patients at 1 year**	**Odds ratio**	**%**		
MTX	405	Reference	–	–	–
MTX + abatacept (IV)	555 (407 to 699)	1.84 (1.01 to 3.42)	98	1	High
MTX + abatacept (SC)	574 (390 to 730)	1.98 (0.94 to 3.97)	97	1	High
MTX + adalimumab	588 (508 to 661)	2.10 (1.52 to 2.87)	>99	4	High
IM/SC MTX + adalimumab	601 (353 to 805)	2.22 (0.80 to 6.06)	94	0	Moderate (imprecision)
MTX + certolizumab	504 (361 to 646)	1.49 (0.83 to 2.68)	93	1	Moderate (study limitations)
MTX + etanercept	671 (578 to 757)	3.00 (2.02 to 4.59)	>99	2	High
MTX + golimumab (SC)	476 (315 to 638)	1.33 (0.68 to 2.59)	83	1	Moderate (study limitations)
MTX + infliximab	580 (470 to 719)	2.03 (1.30 to 3.77)	>99	3	High
MTX + rituximab	622 (469 to 750)	2.42 (1.30 to 4.42)	99	1	High
MTX + tocilizumab (4 mg/kg)	529 (392 to 665)	1.66 (0.95 to 2.92)	97	1	Moderate (study limitations)
MTX + tocilizumab (8 mg/kg)	565 (426 to 696)	1.91 (1.09 to 3.36)	98	2	High
MTX + tofacitinib	674 (416 to 864)	3.04 (1.05 to 9.37)	98	1	Moderate (imprecision)
MTX + ciclosporin	539 (370 to 695)	1.72 (0.86 to 3.36)	94	1	Low (indirectness, imprecision, study limitations)
IM/SC MTX + ciclosporin	516 (234 to 803)	1.57 (0.44 to 6.01)	75	0	Low (imprecision, study limitations)
MTX + hydroxychloroquine/chloroquine	346 (136 to 663)	0.78 (0.23 to 2.90)	35	0	Moderate (imprecision)
MTX + sulfasalazine	427 (219 to 654)	1.10 (0.41 to 2.78)	57	1	Low (indirectness, imprecision, study limitations)
MTX + sulfasalazine + hydroxychloroquine	612 (442 to 765)	2.32 (1.17 to 4.79)	99	0	Moderate (indirectness)
IM/SC MTX	434 (288 to 595)	1.13 (0.59 to 2.16)	65	1	Moderate (study limitations)
Radiographic progression (18 studies; 7594 patients)	**Mean change on Sharp-VdH scale over 1 year (points)**	**Standardized mean difference**	**%**		
MTX	2.34	Reference	–	–	
MTX + abatacept (IV)	1.11 (−1.29 to 3.47)	−0.20 (−0.60 to 0.19)	88	1	Moderate (imprecision)
MTX + adalimumab	0.09 (−1.52 to 1.88)	−0.37 (−0.64 to −0.08)	99	2	High
MTX + certolizumab	−0.01 (−1.74 to 1.74)	−0.39 (−0.68 to −0.10)	99	2	Moderate (study limitations)
MTX + etanercept	0.12 (−1.19 to 1.67)	−0.37 (−0.59 to −0.11)	99	3	High
MTX + golimumab (SC)	1.57 (−0.87 to 4.08)	−0.13 (−0.53 to 0.29)	76	1	Low (study limitations, imprecision)
MTX + infliximab	−0.26 (−2.59 to 2.10)	−0.43 (−0.82 to −0.04)	98	1	High
MTX + rituximab	0.03 (−2.40 to 2.42)	−0.38 (−0.79 to 0.01)	97	1	Moderate (imprecision)
MTX + tocilizumab (4 mg/kg)	0.84 (−1.64 to 3.30)	−0.25 (−0.66 to 0.16)	91	1	Moderate (study limitations)
MTX + tocilizumab (8 mg/kg)	0.14 (−2.28 to 2.54)	−0.37 (−0.77 to 0.03)	97	1	Moderate (study limitations)
MTX + tofacitinib	1.09 (−2.78 to 5.17)	−0.21 (−0.85 to 0.47)	73	1	Moderate (imprecision)
MTX + ciclosporin	1.07 (−0.68 to 2.94)	−0.21 (−0.50 to 0.10)	92	2	Low (study limitations, imprecision)
MTX + sulfasalazine + hydroxychloroquine	2.14 (−2.18 to 6.69)	−0.03 (−0.75 to 0.72)	54	0	Moderate (imprecision)

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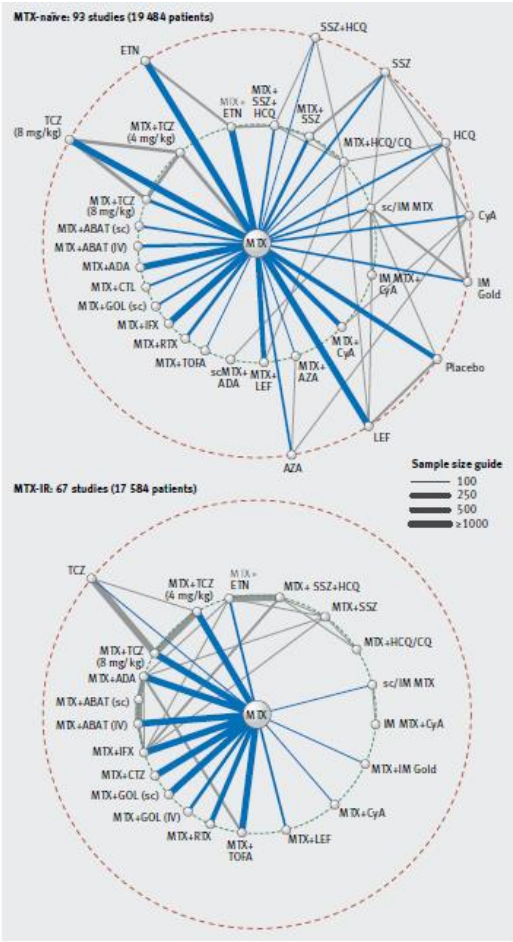
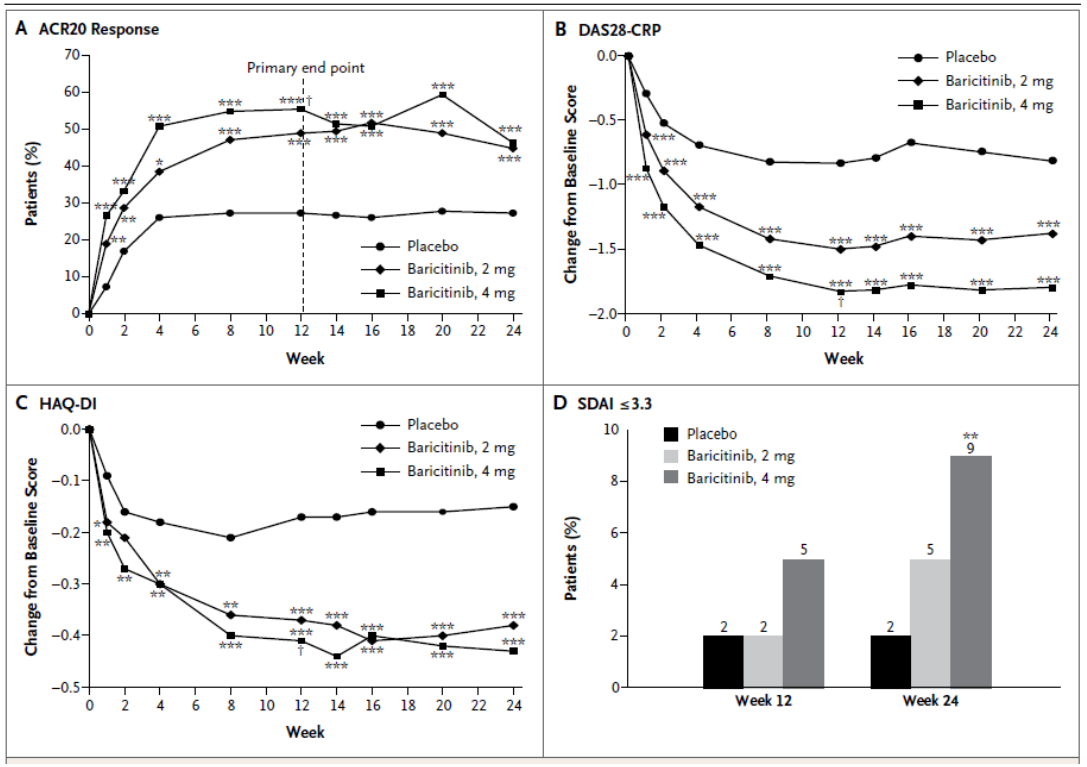
158 trials were included, with between 10 and 53 trials available for each outcome. In methotrexate naive patients, several treatments were statistically superior to oral methotrexate for ACR50 response: sulfasalazine and hydroxychloroquine ("triple therapy"), several biologics (abatacept, adalimumab, etanercept, infliximab, rituximab, tocilizumab), and tofacitinib. The estimated probability of ACR50 response was similar between these treatments (range 56-67%), compared with 41% with methotrexate. Methotrexate combined with adalimumab, etanercept, certolizumab, or infliximab was statistically superior to oral methotrexate for inhibiting radiographic progression, but the estimated mean change over one year with all treatments was less than the minimal clinically important difference of 5 units on the Sharp-van der Heijde scale. Triple therapy had statistically fewer withdrawals due to adverse events than methotrexate plus infliximab. After an inadequate response to methotrexate, several treatments were statistically superior to oral methotrexate for ACR50 response: triple therapy, methotrexate plus hydroxychloroquine, methotrexate plus leflunomide, methotrexate plus intramuscular gold, methotrexate plus most biologics, and methotrexate plus tofacitinib. The probability of response was 61% with triple therapy and ranged widely (27-70%) with other treatments. No treatment was statistically superior to oral methotrexate for inhibiting radiographic progression. Methotrexate plus abatacept had a statistically lower rate of withdrawals due to adverse events than several treatments.



Baricitinib in Patients with Refractory Rheumatoid Arthritis

Mark C. Genovese, M.D., Joel Kremer, M.D., Omid Zamani, M.D., Charles Ludivico, M.D., Marek Krogulec, M.D., Li Xie, M.S., Scott D. Beattie, Ph.D., Alisa E. Koch, M.D., Tracy E. Cardillo, M.S., Terence P. Rooney, M.D., William L. Macias, M.D., Ph.D., Stephanie de Bono, M.D., Ph.D., Douglas E. Schlichting, M.S., and Josef S. Smolen, M.D.

In this phase 3 study involving 527 patients with an inadequate response to or unacceptable side effects associated with one or more tumor necrosis factor inhibitors, other biologic DMARDs, or both, we randomly assigned the patients in a 1:1:1 ratio to baricitinib at a dose of 2 or 4 mg daily or placebo for 24 weeks. End points, tested hierarchically at week 12 to control type 1 error, were the American College of Rheumatology 20% (ACR20) response (primary end point), the Health Assessment Questionnaire–Disability Index (HAQ-DI) score, the 28-joint Disease Activity Score based on C-reactive protein level (DAS28-CRP), and a Simplified Disease Activity Index (SDAI) score of 3.3 or less (on a scale of 0.1 to 86.0, with a score of 3.3 or less indicating remission). Comparisons with placebo were made first with the 4-mg dose of baricitinib and then with the 2-mg dose.



Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial

Iain B McInnes, Philip J Mease, Bruce Kirkham, Arthur Kavanaugh, Christopher T Ritchlin, Proton Rahman, Désirée van der Heijde, Robert Landewé, Philip G Conaghan, Alice B Gottlieb, Hanno Richards, Luminita Pricop, Gregory Ligozio, Manmath Patekar, Shephard Mpofu, on behalf of the FUTURE 2 Study Group

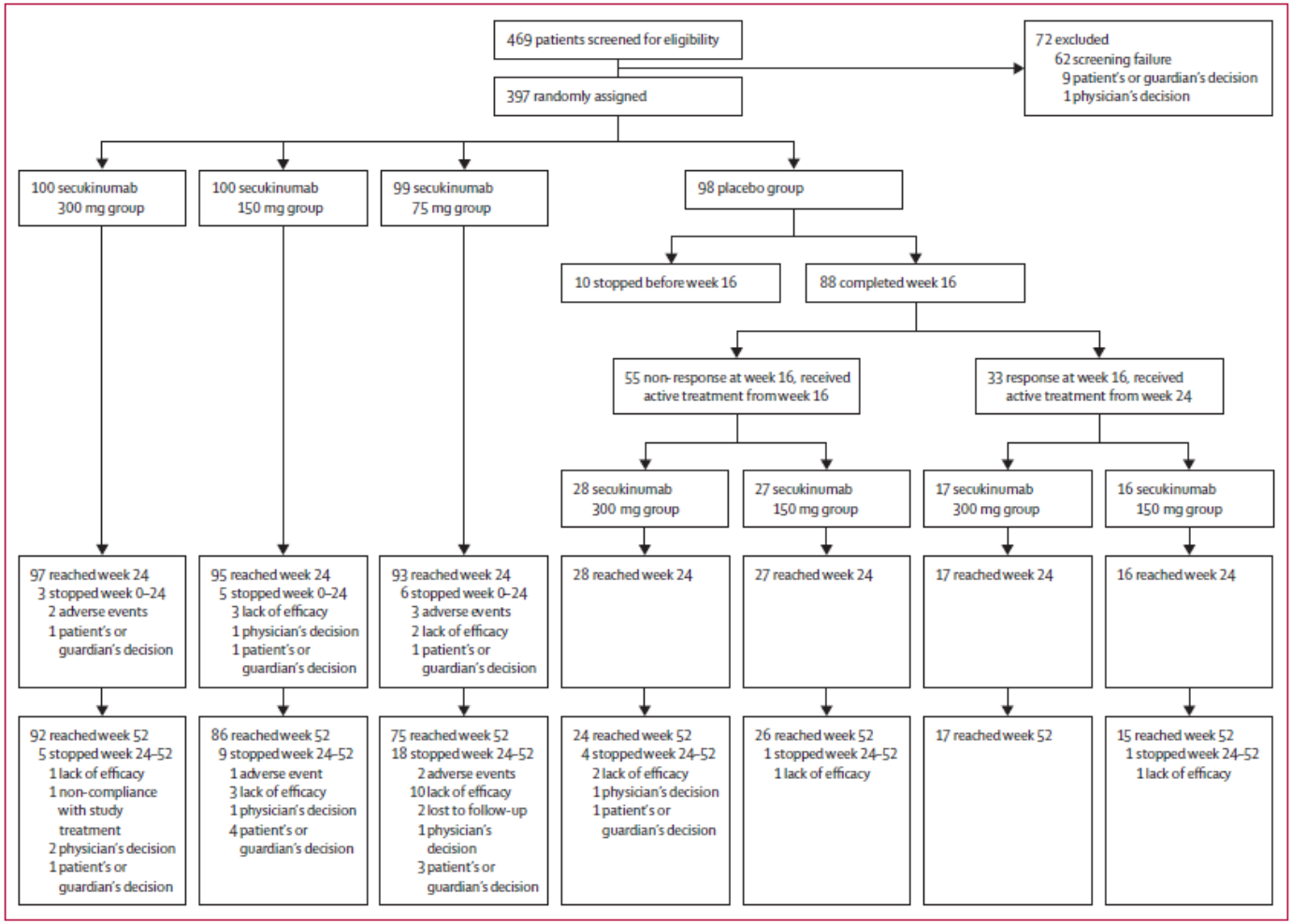


Figure 1: **Trial profile**
All patients who were randomly allocated to treatment were included in the analysis of the prespecified primary and secondary endpoints at week 24.

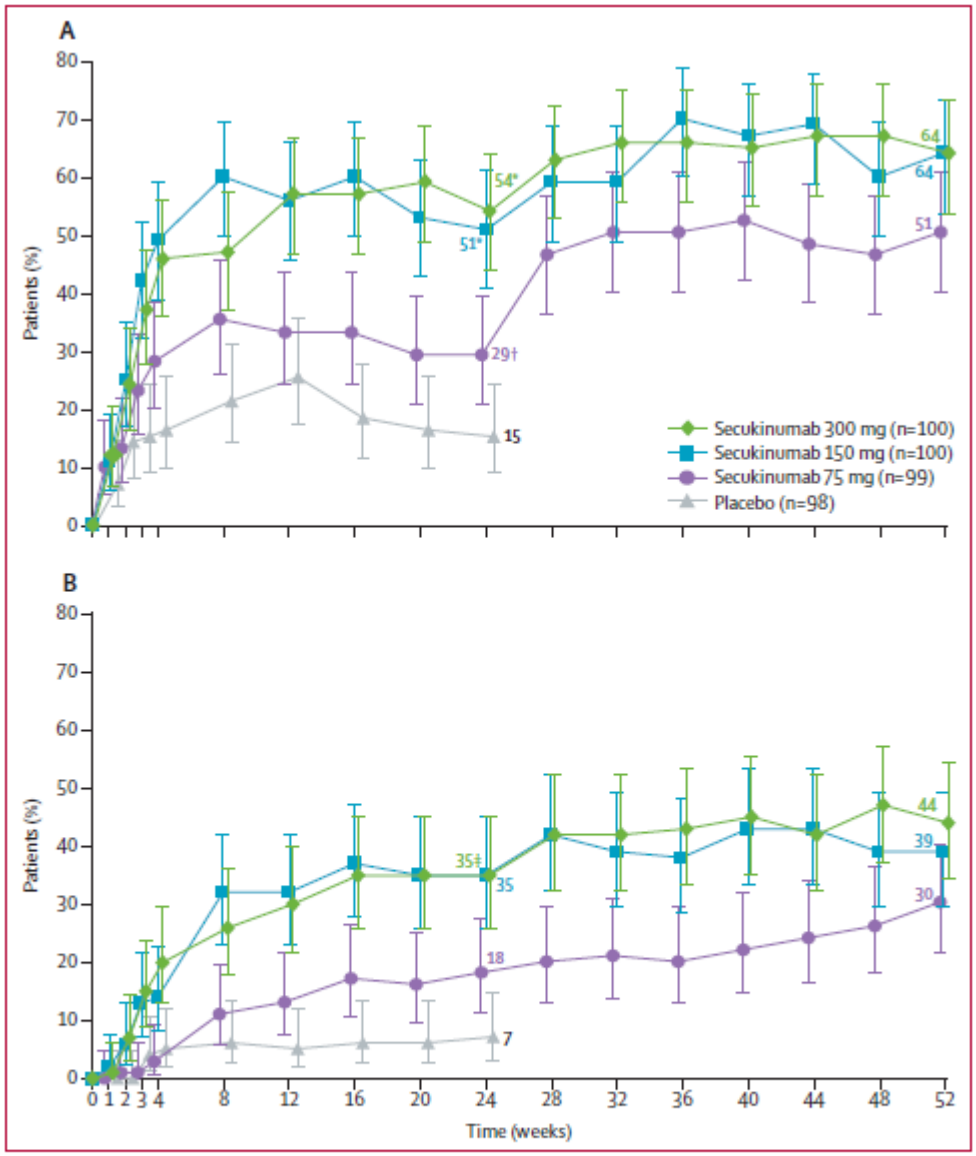


***Figure 2*: ACR20 (A) and ACR50 (B) response rates from baseline to week 52**

Missing data were imputed as non-response until week 52. p values at week 24 were analysed as part of the statistical hierarchy and were adjusted for multiplicity of testing. Response rates over time are presented for patients according to their treatment group at randomisation. ACR20=at least 20% improvement in the American College of Rheumatology response criteria. ACR50=at least 50% improvement in the American College of Rheumatology response criteria. *p<0·0001 versus placebo. †p<0·05 versus placebo. ‡p<0·01 versus placebo.

	Secukinumab 300 mg (n=100)			Secukinumab 150 mg (n=100)			Secukinumab 75 mg (n=99)			Secukinumab (pooled data)			Placebo (n=98)
	Value*	Effect size versus placebo (95% CI)	p value versus placebo	Value*	Effect size versus placebo (95% CI)	p value versus placebo	Value*	Effect size versus placebo (95% CI)	p value versus placebo	Value*	Effect size versus placebo (95% CI)	p value versus placebo	Value*
ACR20	54/100 (54%)	OR 6·81 (3·42 to 13·56)	<0·0001	51/100 (51%)	OR 6·52 (3·25 to 13·08)	<0·0001	29/99 (29%)	OR 2·32 (1·14 to 4·73)	0·0399	..	..	..	15/98 (15%)
PASI75†	26/41 (63%)	OR 9·48 (3·33 to 27·00)	<0·0001	28/58 (48%)	OR 5·70 (2·12 to 15·34)	0·0017	14/50 (28%)	OR 2·07 (0·74 to 5·81)	0·1650	..	..	..	7/43 (16%)
PASI90†	20/41 (49%)	OR 10·74 (3·13 to 36·84)	0·0005	19/58 (33%)	OR 6·36 (1·89 to 21·47)	0·0057	6/50 (12%)	OR 1·38 (0·36 to 5·36)	0·6421	..	..	..	4/43 (9%)
DAS28-CRP	−1·61 (0·11)	Difference −0·65 (−1·02 to −0·29)	0·0013	−1·58 (0·11)	Difference −0·62 (−0·98 to −0·26)	0·0057	−1·12 (0·11)	Difference −0·16 (−0·53 to 0·20)	0·6421	..	..	..	−0·96 (0·15)
SF36-PCS	7·25 (0·74)	Difference 5·30 (2·91 to 7·69)	0·0013	6·39 (0·73)	Difference 4·44 (2·05 to 6·83)	0·0057	4·38 (0·75)	Difference 2·42 (0·02 to 4·83)	0·6421	..	..	..	1·95 (0·97)
HAQ-DI	−0·56 (0·05)	Difference −0·25 (−0·40 to −0·10)	0·0040	−0·48 (0·05)	Difference −0·17 (−0·32 to −0·02)	0·0555	−0·32 (0·05)	Difference −0·01 (−0·16 to 0·15)	0·9195	..	..	..	−0·31 (0·06)
ACR50	35/100 (35%)	OR 7·15 (2·97 to 17·22)	0·0040	35/100 (35%)	OR 7·54 (3·11 to 18·25)	0·0555	18/99 (18%)	OR 2·91 (1·15 to 7·36)	0·9195	..	..	..	7/98 (7%)
Resolution of dactylitis‡	..	..	..	..	..	..	..	..	..	52/111 (47%)	OR 4·35 (1·39 to 14·29)	0·9195	4/27 (15%)
Resolution of enthesitis‡	..	..	..	..	..	..	..	..	..	76/188 (40%)	OR 2·56 (1·30 to 5·00)	0·9195	14/65 (22%)

Least-squares mean and 95% CI are from a mixed-model repeated measures with treatment regimen, analysis visit, and randomisation stratum (anti-TNF-naive or anti-TNF-IR) as factors, weight and baseline score as continuous covariates, and treatment by analysis visit and baseline score by analysis visit as interaction terms, and an unstructured covariance structure. OR and 95% CI are from a logistic regression model with treatment and randomisation stratum (anti-TNF-naive or anti-TNF-IR) as factors and baseline weight as a covariate; OR greater than 1 favours secukinumab. All p values are versus placebo and are adjusted for multiplicity. ACR20=at least 20% improvement in the American College of Rheumatology. OR=odds ratio. PASI=Psoriasis Area and Severity Index. DAS28-CRP=28-joint Disease Activity Score using C-Reactive Protein. SF36-PCS=36-item Short Form Health Survey. HAQ-DI=Health Assessment Questionnaire Disability Index. ACR50=at least 50% improvement in the American College of Rheumatology. Anti-TNF-IR=inadequate response to a tumour necrosis factor drug or treatment stopped because of safety or tolerability reasons. *Data are n/N (%) or least-squares mean (SE). †Assessed in patients with psoriasis on at least 3% of their body surface area. ‡Resolution of dactylitis and enthesitis was assessed only in patients with these symptoms at baseline; pooled data are reported for secukinumab 300 mg, 150 mg, and 75 mg.

Table 2: **Comparison of secukinumab versus placebo at week 24 for prespecified primary and secondary endpoints**

	Secukinumab 300 mg			Secukinumab 150 mg			Secukinumab 75 mg			Placebo
	Value*	Odds ratio versus placebo (95% CI)	p value versus placebo	Value*	Odds ratio versus placebo (95% CI)	p value versus placebo	Value*	Odds ratio versus placebo (95% CI)	p value versus placebo	
Anti-TNF-naive patients										
ACR20 response	39/67 (58%)	7·77 (3·36–17·98)	<0·0001	40/63 (63%)	9·99 (4·22–23·66)	<0·0001	24/65 (37%)	3·17 (1·36–7·40)	0·0075	10/63 (16%)
ACR50 response	26/67 (39%)	9·72 (3·14–30·09)	<0·0001	28/63 (44%)	12·54 (4·03–39·05)	<0·0001	16/65 (25%)	4·90 (1·53–15·64)	0·0074	4/63 (6%)
ACR70 response	15/67 (22%)	NE	0·0003	17/63 (27%)	NE	<0·0001	4/65 (6%)	NE	0·3654	1/63 (2%)
PASI75 response†	19/30 (63%)	7·96 (2·42–26·16)	0·0006	20/36 (56%)	6·33 (1·99–20·15)	0·0018	10/33 (30%)	1·94 (0·59–6·34)	0·2729	6/31 (19%)
PASI90 response†	16/30 (53%)	13·11 (3·09–55·59)	0·0005	14/36 (39%)	8·09 (1·92–34·09)	0·0044	4/33 (12%)	1·40 (0·28–7·02)	0·6825	3/31 (10%)
Anti-TNF-IR patients										
ACR20 response	15/33 (45%)	4·97 (1·53–16·15)	0·0077	11/37 (30%)	2·55 (0·78–8·32)	0·1216	5/34 (15%)	1·03 (0·27–3·95)	0·9639	5/35 (14%)
ACR50 response	9/33 (27%)	4·37 (1·05–18·26)	0·0431	7/37 (19%)	2·39 (0·56–10·15)	0·2374	2/34 (6%)	0·69 (0·11–4·42)	0·6941	3/35 (9%)
ACR70 response	5/33 (15%)	NE	0·0228	4/37 (11%)	NE	0·1151	2/34 (6%)	NE	0·2391	0/35 (0%)
PASI75 response†	7/11 (64%)	19·29 (1·77–210·18)	0·0152	8/22 (36%)	6·17 (0·66–57·30)	0·1094	4/17 (24%)	3·46 (0·33–36·06)	0·2986	1/12 (8%)
PASI90 response†	4/11 (36%)	6·43 (0·58–70·74)	0·1282	5/22 (23%)	3·50 (0·35–34·91)	0·2859	2/17 (12%)	1·37 (0·11–17·30)	0·8098	1/12 (8%)

Data are n/N (%), unless otherwise indicated. p values not adjusted for multiplicity of testing. ACR20=at least 20% improvement in the American College of Rheumatology. ACR50=at least 50% improvement in the American College of Rheumatology. ACR70=at least 70% improvement in the American College of Rheumatology. NE=not estimable. PASI=Psoriasis Area and Severity Index. Anti-TNF-IR=inadequate response to a tumour necrosis factor agent or stopped treatment because of safety or tolerability reasons. *Missing data were imputed as non-response. †Assessed in patients with psoriasis on at least 3% of their body surface area at baseline.

Table 3: **Efficacy of secukinumab at week 24 in anti-TNF-naive and anti-TNF-IR patients in a prespecified exploratory analysis**

Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial

Laura C Coates, Anna R Moverley, Lucy McParland, Sarah Brown, Nuria Navarro-Coy, John L O'Dwyer, David M Meads, Paul Emery, Philip G Conaghan, Philip S Helliwell**

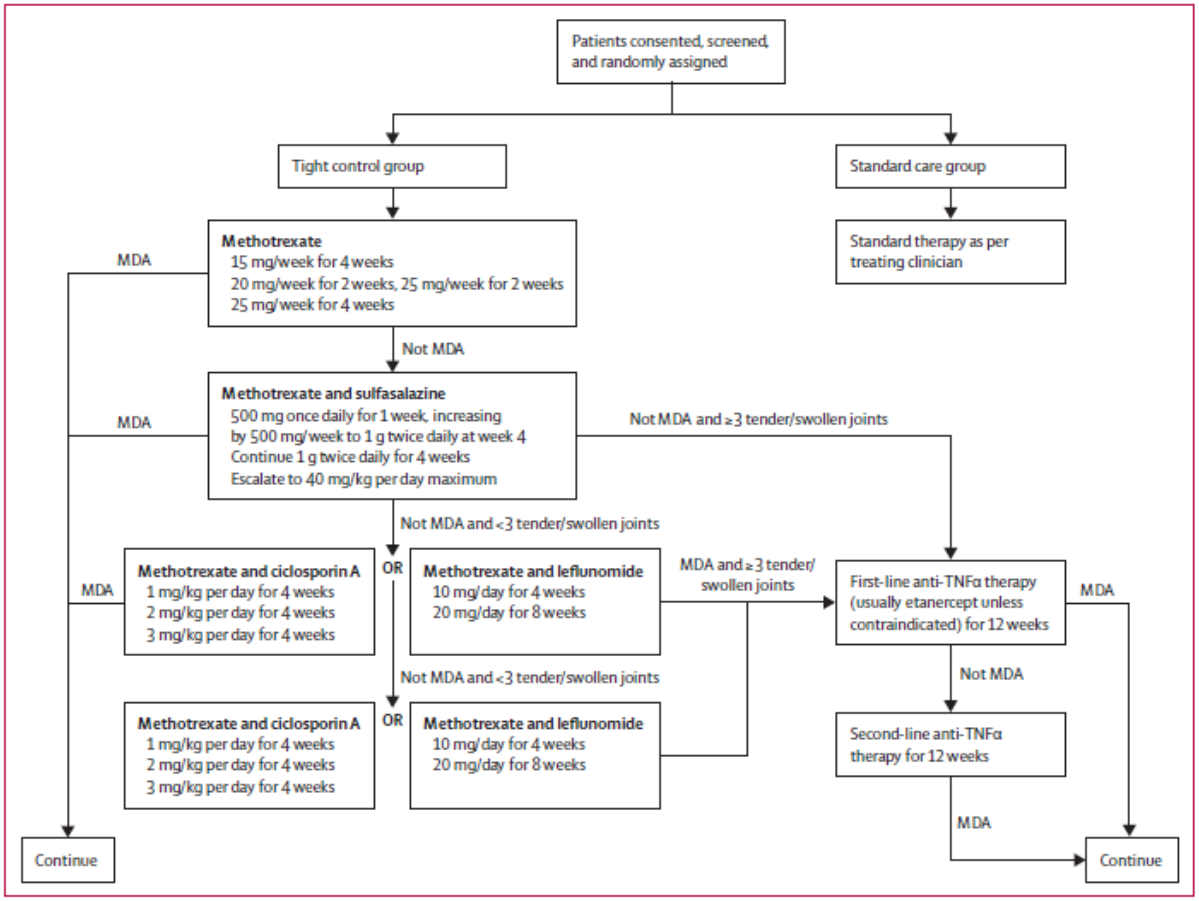


Figure 1: **Treatment protocol**
MDA=minimal disease activity. TNF=tumour necrosis factor.

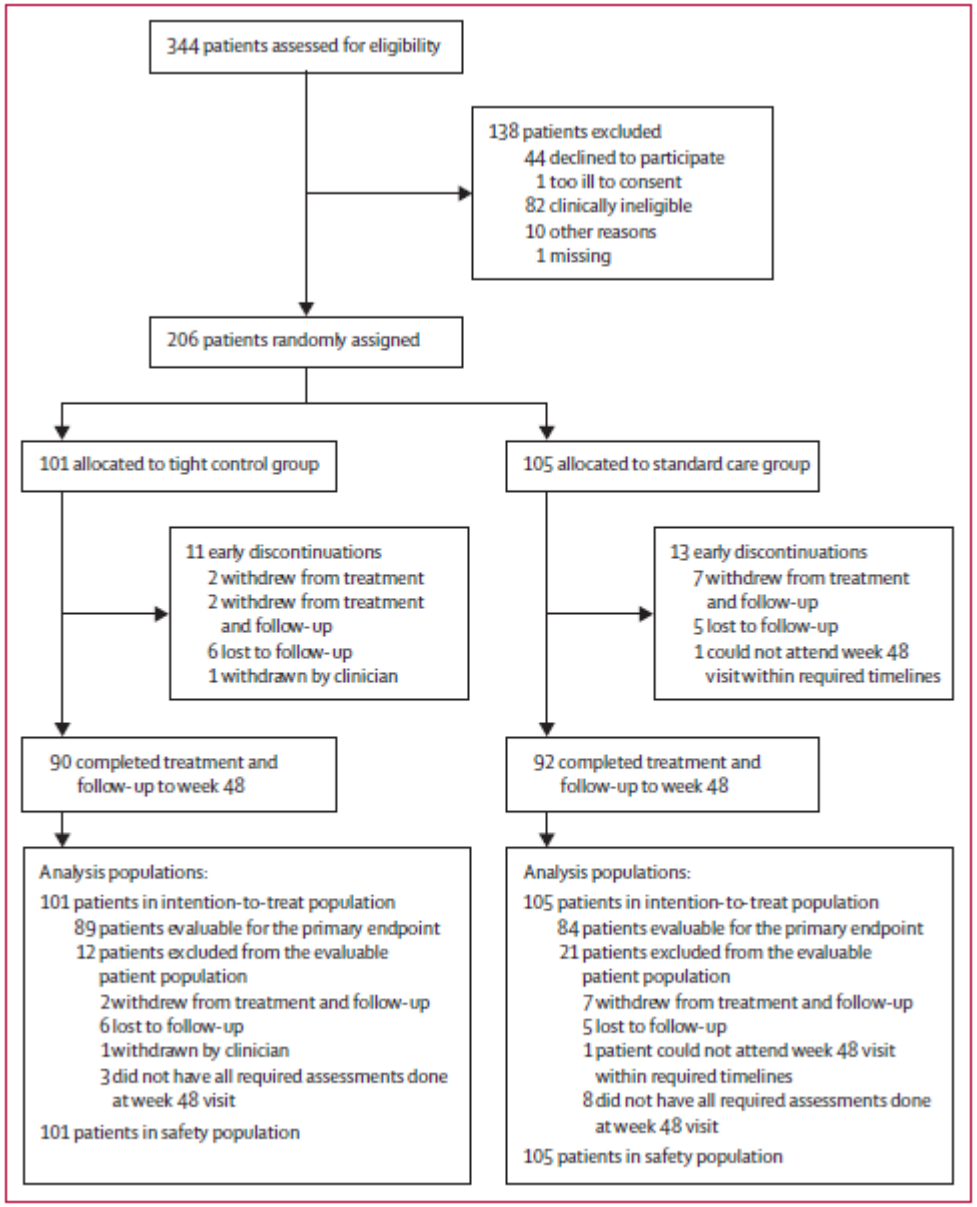


Figure 2: **Trial profile**

	Odds ratio (95% CI)	p value
Treatment group: tight control vs standard care	1·91 (1·03–3·55)	0·0392
Arthritis type: oligoarthritis vs polyarthritis	0·62 (0·31–1·24)	0·1733
Centre: other sites vs Chapel Allerton Hospital	2·33 (0·87–6·27)	0·0929
Centre: St Luke's Hospital Bradford vs Chapel Allerton Hospital	0·93 (0·41–2·09)	0·8607
Centre: York District Hospital vs Chapel Allerton Hospital	0·50 (0·17–1·52)	0·2223

ACR20=American College of Rheumatology 20% response. This analysis was done on the intention-to-treat population with multiple imputation. Following multiple imputation of the 206 patients, two patients had an undefined relative improvement for the Health Assessment Questionnaire, which was needed to ascertain the ACR20 value. Other sites were: Harrogate District Hospital, Manchester Royal Infirmary, St Bartholomew's Hospital, North Tyneside General Hospital, and Royal National Hospital for Rheumatic Diseases. These smaller recruiting sites were combined to prevent model convergence problems.

Table 2: **Multivariable logistic regression analysis for the effect of treatment on the primary endpoint (ACR20 at 48 weeks post randomisation)**

	Tight control	Standard care	% difference in proportions (95% CI)	p value
ACR20	55/89 (62%)	37/84 (44%)	17·8% (3·1–32·4)	0·0194
ACR50	44/86 (51%)	21/84 (25%)	26·2% (12·1–40·2)	0·0004
ACR70	33/87 (38%)	15/86 (17%)	20·5% (7·5–33·5)	0·0026
PASI75	44/75 (59%)	27/81 (33%)	25·3% (10·2–40·5)	0·0015

Data are n/N (%) unless otherwise indicated. ACR=American College of Rheumatology. PASI=Psoriasis Area Severity Index.

Table 3: **Univariable analysis (χ^2 test of independence) for the proportion of patients in the evaluable patient population achieving a response at 48 weeks post randomisation for the key secondary endpoints**

Findings Between May 28, 2008, and March 21, 2012, 206 eligible patients were enrolled and randomly assigned to receive tight control (n=101) or standard care (n=105). In the intention-to-treat patient population, the odds of achieving an ACR20 response at 48 weeks were higher in the tight control group than in the standard care group (odds ratio 1·91, 95% CI 1·03–3·55; p=0·0392). Serious adverse events were reported by 20 (10%) patients (25 events in 14 [14%] patients in the tight control group and eight events in six [6%] patients in the standard care group) during the course of the study. No unexpected serious adverse events or deaths occurred.

Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study

Valérie Devauchelle-Pensec[1,3], Jean Marie Berthelot[2], Divi Cornec[1,3], Yves Renaudineau[3], Thierry Marhadour[1], Sandrine Jousse-Joulin[1,3], Solène Querellou[4], Florent Garrigues[5], Michel De Bandt[6], Maelenn Gouillou[7], Alain Saraux[1,3]

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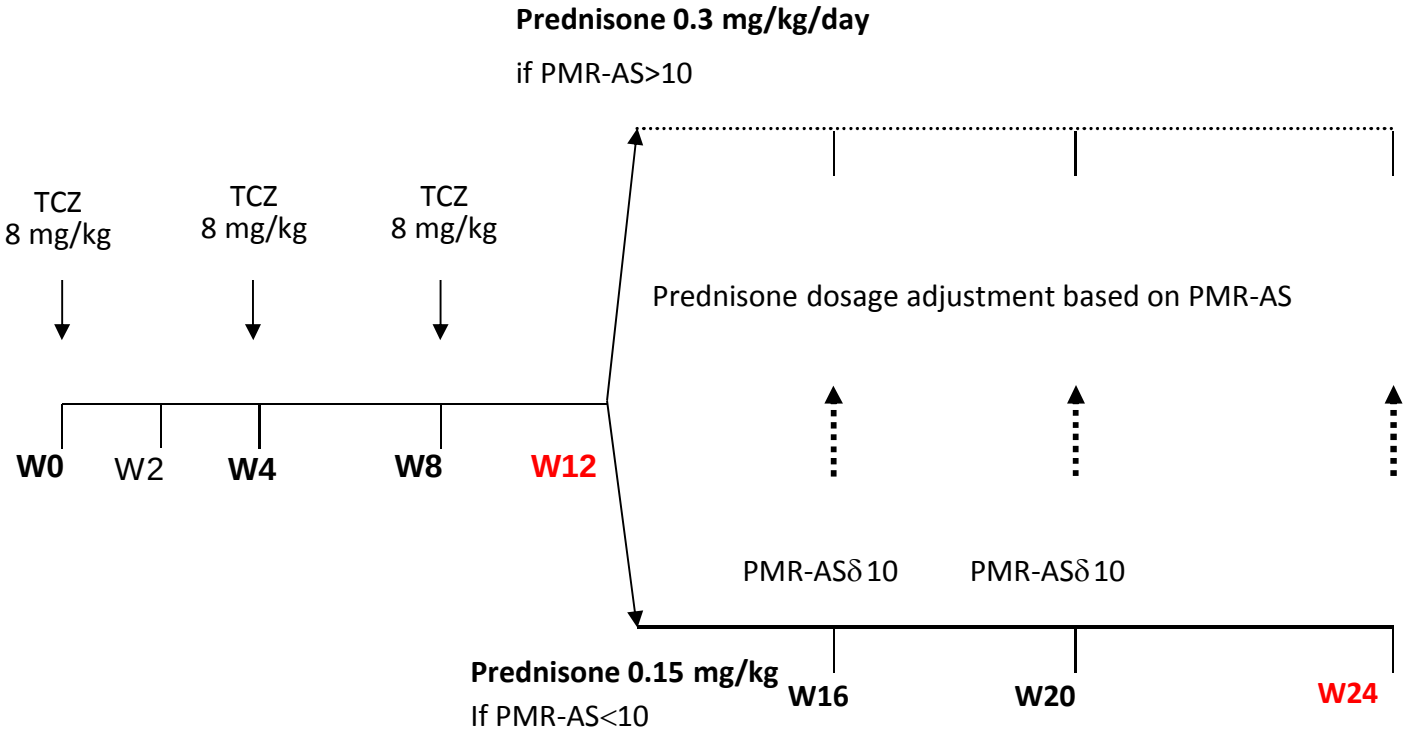
ORIGINAL ARTICLE

Value of ^{18}F-FDG PET/CT for therapeutic assessment of patients with polymyalgia rheumatica receiving tocilizumab as first-line treatment

X. Palard-Novello[1] · S. Querellou[1,5] · M. Gouillou[2] · A. Saraux[3,6] · T. Marhadour[3] · F. Garrigues[4] · R. Abgral[1,5] · P. Y. Salaün[1,5] · V. Devauchelle-Pensec[3,6]



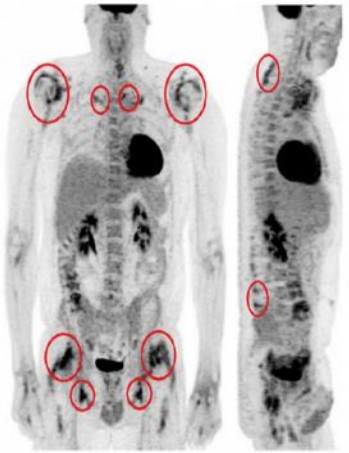


Fig. 1 Maximum intensity projection ^{18}F-FDG PET/CT images. SUVmax measurements were obtained in the ten regions of interest (*red circles*)

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OPEN ACCESS

CONCISE REPORT

Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study

Median, IQR	Week 0	Week 2	Week 4	Week 8	Week 12	p Value Week 0 vs week 12
PMR-AS	36.6 (30.4–43.8)	19.7 (14.9–27.7)	11.0 (7.9–19.3)	5.8 (3.7–11.6)	4.5 (3.2–6.8)	<0.001*
CRP, mg/dL	65.1 (21.6–127.8)	0.5 (0.3–1.4)	0.6 (0.3–3.5)	0.6 (0.2–1.2)	0.2 (0.1–1.0)	<0.001*
ESR, mm/h	51.0 (34.0–79.5)	7.5 (4.0–9.5)	5.0 (4.0–10.0)	4.5 (2.0–5.0	2.00 (2.0–4.5)	<0.001*
Patient VAS for pain	6.4 (4.6–7.8)	5.4 (3.8–6.9)	4.5 (3.2–5.4)	2.2 (1.5–4.2)	1.7 (0.6–2.7)	<0.001*
Patient VAS for fatigue	5.4 (2.9–6.9)	5.3 (3.0–6.2)	4.5 (2.0–5.1)	2.8 (1.0–4.8)	2.1 (0.7–4.4)	<0.001*
Patient VAS for disease activity	6.6 (4.8–7.5)	5.45 (3.8–6.9)	4.5 (3.1–5.4)	2.2 (1.5–4.2)	2.0 (0.9–3.6)	<0.001*
Physician VAS for disease activity	6.8 (6.0–7.9)	4.4 (2.8–6.6)	2.7 (1.7–4.5)	2.1 (0.5–3.1)	1.1 (0.8–1.8)	<0.001*
MST (min)	180.0 (75.0–180.0)	60.0 (60.0–120.0)	30.0 (7.50–60.0)	5.0 (0.0–22.5)	4.0 (0.0–10.0)	<0.001*
EUL	0.5 (0.0–2.0)	0.0 (0.0–2.0)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.002*
0	10 (50.0%)	11 (55.0%)	13 (65.0%)	17 (85.0%)	18 (90.0%)	
1	2 (10.0%)	3 (15.0%)	4 (20.0%)	2 (10.0%)	2 (10.0%)	
2	8 (40.0%)	6 (30.0%)	3 (15.0%)	1 (5.0%)	0 (0.0%)	
3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
PMR-AS (ESR)	35.6 (30.4–39.9)	20.8 (15.3–29.4)	13.7 (9.3–22.0)	5.8 (3.5–11.8)	4.7 (3.5–6.6)	<0.001*

V Devauchelle-pensec et al, Ann Rheum Dis 2016

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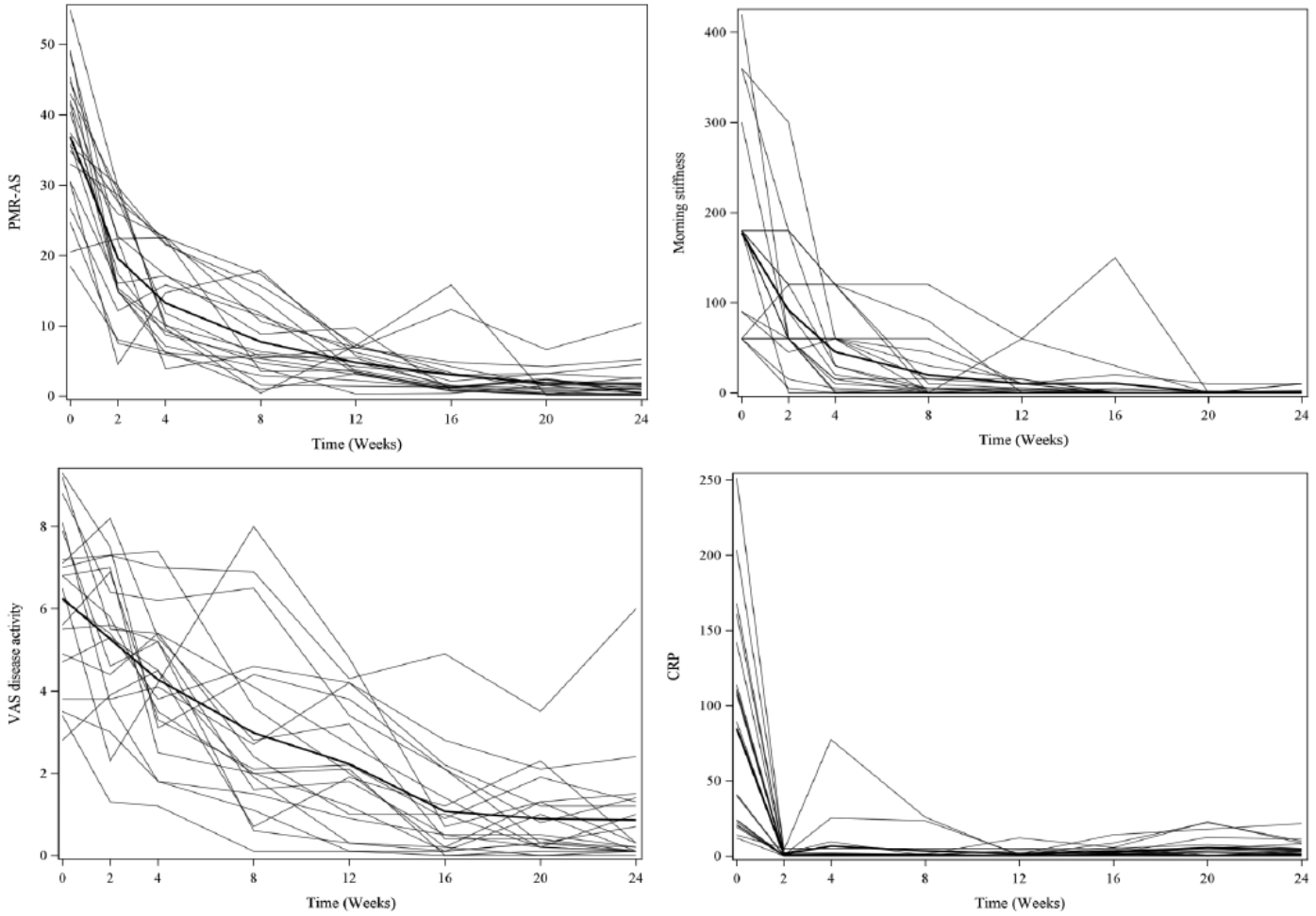
CONCISE REPORT

Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study



V Devauchelle-pensec et al, Ann Rheum Dis 2016

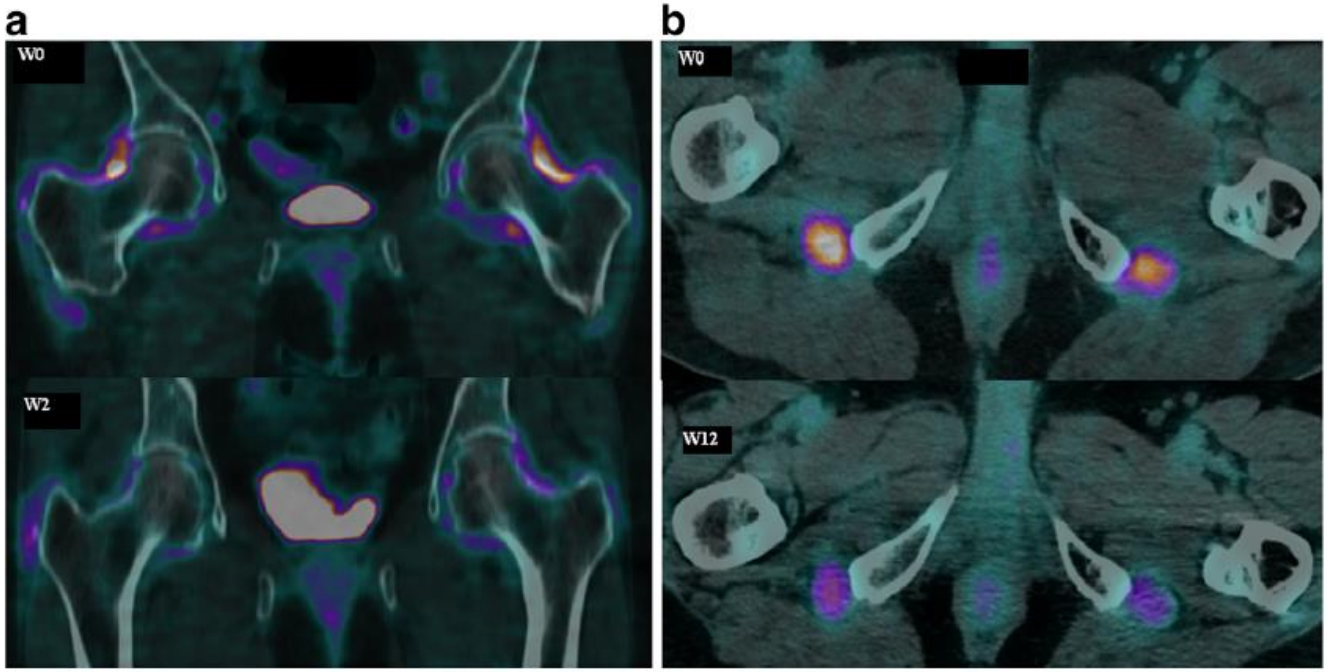


Fig. 2 Changes in FDG uptake on follow-up PET/CT imaging. **a** Coronal images of the hip region before treatment (week 0, *W0*) and after one infusion of tocilizumab (week 2, *W2*) in a 73-year-old woman with polymyalgia rheumatica. At week 0, the right hip SUVmax is 12.3 and the left hip SUVmax is 9.7. At week 2, the right hip SUVmax is 10.1 and the left hip SUVmax is 9.4. **b** Axial images of the ischial tuberosity region before treatment (week 0, *W0*) and after two infusions of tocilizumab (week 12, *W12*) in a 60-year-old man with polymyalgia rheumatica. At week 0, the right ischial tuberosity SUVmax is 8.5 and the left ischial tuberosity SUVmax is 9.8. At week 2, the right ischial tuberosity SUVmax is 5 and the left ischial tuberosity region SUVmax is 5.5

Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial

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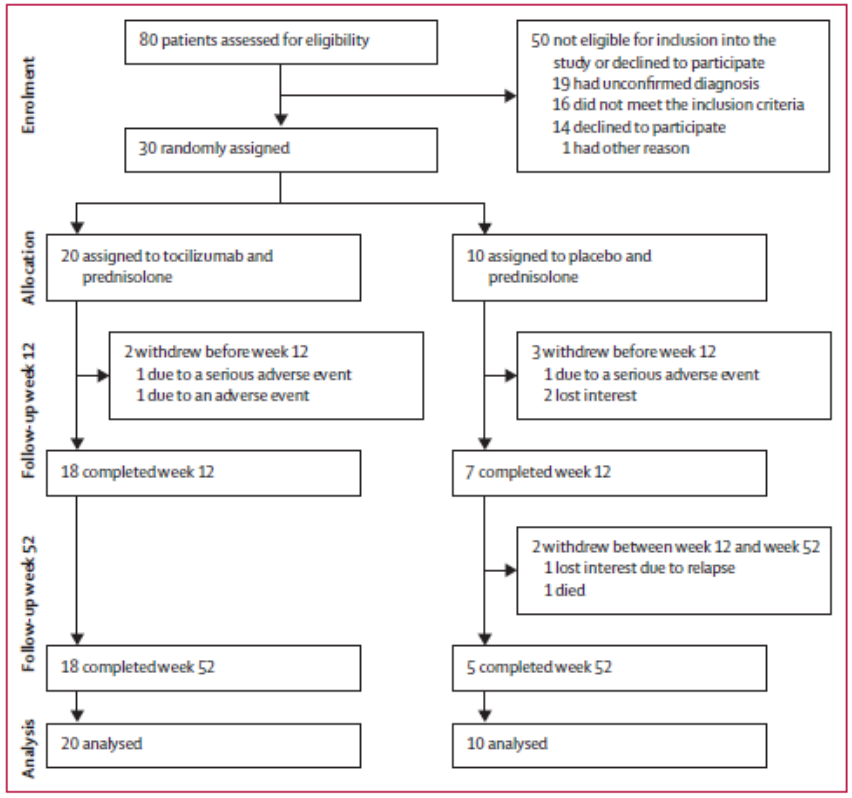

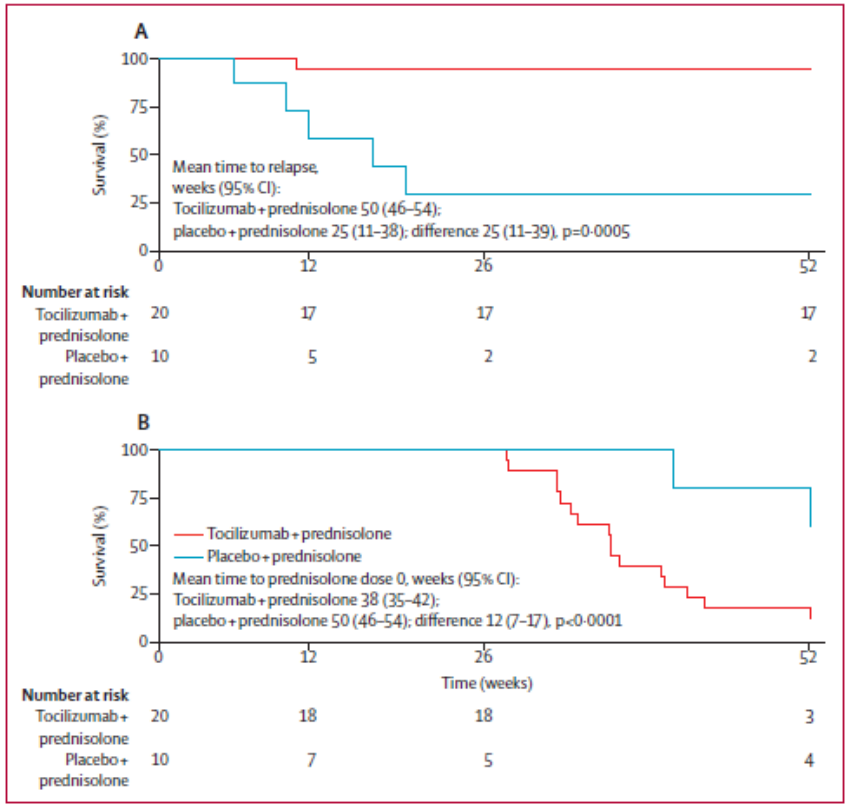

Figure 2: **Kaplan-Meier curve for relapse-free survival through to week 52 (A) and the time to taper down prednisolone to 0 mg per day (B)**

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	Tocilizumab plus prednisolone (N=20)	Placebo plus prednisolone (N=10)	Risk difference (95% CI)	p value
Endpoints				
Complete remissions				
After 12 weeks	17 (85%)	4 (40%)	45% (11 to79)	0·0301
After 52 weeks	17 (85%)	2 (20%)	65% (36 to 94)	0·0010
Patients whose prednisolone dose tapered to 0 mg per day	16 (80%)	2 (20%)	60% (30 to 90)	0·0041
Cumulative prednisolone dose (mg/kg)				
After 12 weeks	34 (32 to 35)	36 (34 to 39)	..	0·0477
After 26 weeks	41 (39 to 46)	66 (52 to 75)	..	0·0015
After 52 weeks	43 (39 to 52)	110 (88 to 150)	..	0·0005
Patients with any adverse event	15 (75%)	7 (70%)	5% (–29 to 39)	1·00
Patients with a serious adverse event	7 (35%)	5 (50%)	–15% (–52 to 22)	0·46
First relapse*				
Timepoint of first relapse (weeks)	11·0	12·0 (10·1 to 17·1)	..	0·77
Prednisolone dose at first relapse (mg/kg per day)	0·11	0·10 (0·09 to 0·17)	..	0·77
Erythrocyte sedimentation rate at first relapse (mm/h)	2·00	20·0 (10·0 to 30·0)	..	0·14
C-reactive protein concentration at first relapse (mg/L)	3·00	16·0 (11·0 to 25·0)	..	0·23

Data are n (%) or median (IQR) unless stated otherwise. *One patient in the tocilizumab group and five in the placebo group had first relapse.

Table 2: **Treatment effect on primary and secondary endpoints**

Ustekinumab for the treatment of refractory giant cell arteritis

Table 1 Characteristics and prior treatment of 14 patients with Giant Cell Arteritis (GCA), treated with ustekinumab

Age, years, mean (SD)	69.6 (8.6)
Female, n (%)	11/14 (79)
Met 1990 ACR criteria for GCA, n (%)	14/14 (100)
Biopsy positive, n (%)	9/14 (64)
Temporal artery ultrasound positive, n (%)	3/10 (30)
CT Angiogram positive, n (%)	7/10 (70)
Cranial ischaemic complications, n (%)	3 (21%)
Vasculitis damage index, median (IQR)	2 (0, 2)
Charlson comorbidity index, median (IQR)	1 (1, 2)
Disease duration, months, median (IQR)	29.5 (12.8, 45.5)
Relapses, median (IQR)	2 (2, 4.3)
Clinical presentation at last relapse	
Cranial, n (%)	8 (57)
Polymyalgia rheumatica, n (%)	6 (43)
Constitutional, n (%)	6 (43)
Large vessel vasculitis, n (%)	5 (36)
Prior treatment	
Glucocorticoids, n (%)	14 (100)
Glucocorticoid adverse events, n (%)	12 (86)
Other immunosuppressants, n (%)	12 (86)
Other immunosuppressants failed, median (range)	1 (0, 3)
Methotrexate, n (%)	11 (83)
Duration of methotrexate, months, median (IQR)	10 (5, 36)
Dose of methotrexate, mg/week, median (IQR)	20 (15, 21)
Azathioprine	2 (14)
Leflunomide	1 (7)
Adalimumab	1 (7)

Table 2 Outcome measures pre-ustekinumab and at last follow-up (median follow-up of 13.5 months (range 7–26) after initiation of ustekinumab)

Outcome	Pre-ustekinumab	Last follow-up	p Value
Prednisolone dose, mg, median (IQR)	20 (15, 25)	5 (2.9, 8.1)	0.001
ESR, mm/h, median (IQR)	14 (5.8, 29.3)	15 (9.8, 28.5)	0.572
CRP, mg/L, median (IQR)	12.2 (3.4, 21)	4.8 (2.8, 15)	0.177
Stopped glucocorticoids, n (%)	–	4 (29)	–
Stopped other immunosuppressants, n (%)	–	11 (92)	–

CRP, C reactive protein, normal range 0–5 mg/L; ESR, erythrocyte sedimentation rate, normal range 0–30 mm/h.

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Fièvre périodique autoinflammatoires (familial Mediterranean fever; mevalonate kinase deficiency; TNF receptor-associated periodic fever syndrome; cryopyrin-associated periodic syndromes)

Evidence-based provisional clinical classification criteria for autoinflammatory periodic fevers

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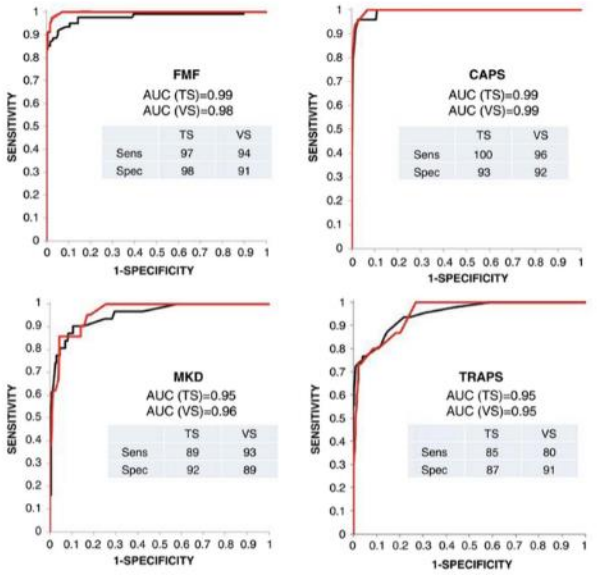


Figure 1 Receiver operating characteristic curves obtained for training (TS) and validation (VS) sets of gold standard patients, and the sensitivity (Sens) and specificity (Spec) of each classification criterion. AUC, area under the curve; CAPS, cryopyrin-associated periodic syndromes; FMF, familial Mediterranean fever; MKD, mevalonate kinase deficiency; TRAPS, receptor-associated periodic fever syndrome.

The reference 'gold standard' group includes patients with FMF, TRAPS, CAPS or MKD with a confirmatory molecular analysis[14] defined as follows:

- FMF: two *MEFV* mutations, of which at least one is in exon 10[23];
- MKD: two *MVK* mutations with the exclusion of variants with an uncertain pathological role (such as S52N P165L, H20Q) (http://fmf.igh.cnrs.fr/infevers/)[23];
- TRAPS: heterozygous *TNFRSF1A* mutations with the exclusion of low-penetrance (such as R92Q or P46L) or uncertain mutations (http://fmf.igh.cnrs.fr/infevers/)[23];
- CAPS: heterozygous *NLRP3* mutations with the exclusion of low-penetrance variants (V198M), functional polymorphisms (Q703K) or variants with uncertain pathological role (http://fmf.igh.cnrs.fr/infevers/).[23]

Federici S, *et al. Ann Rheum Dis* 2015;**74**:799–805.

Leading to these four classification criteria, with a scoring for presence or absence

Table 3 The Eurofever clinical diagnostic/classification criteria*

FMF		MKD		CAPS		TRAPS	
Presence	**Score**	**Presence**	**Score**	**Presence**	**Score**	**Presence**	**Score**
Duration of episodes < 2 days	9	Age at onset <2 years	10	Urticarial rash	25	Periorbital oedema	21
Chest pain	13	Aphthous stomatitis	11	Neurosensorial hearing loss	25	Duration of episodes >6 days	19
Abdominal pain	9	Generalised enlargement of lymph nodes or splenomegaly	8	Conjunctivitis	10	Migratory rash†	18
Eastern Mediterranean‡ ethnicity	22	Painful lymph nodes	13			Myalgia	6
North Mediterranean‡ ethnicity	7	Diarrhoea (sometimes/often)	20			Relatives affected	7
		Diarrhoea (always)	37				
Absence		**Absence**		**Absence**		**Absence**	
Aphthous stomatitis	9	Chest pain	11	Exudative pharyngitis	25	Vomiting	14
Urticarial rash	15			Abdominal pain	15	Aphthous stomatitis	15
Enlarged cervical lymph nodes	10						
Duration of episodes >6 days	13						
Cut-off	≥60	Cut-off	≥42	Cut-off	≥52	Cut-off	≥43

*The clinical features should be related to the typical fever episodes (ie, exclusion of intercurrent infection or other comorbidities). †Centrifugal migratory, erythematous patches most typically overlying a local area of myalgia, usually on the limbs or trunk.
‡Eastern Mediterranean: Turkish, Armenian, non-Ashkenazi Jewish, Arab. North Mediterranean: Italian, Spanish, Greek.
CAPS, cryopyrin-associated periodic syndromes; FMF, familial Mediterranean fever; MKD, mevalonate kinase deficiency; TRAPS, receptor-associated periodic fever syndrome.

Federici S, *et al*. *Ann Rheum Dis* 2015;**74**:799–805.

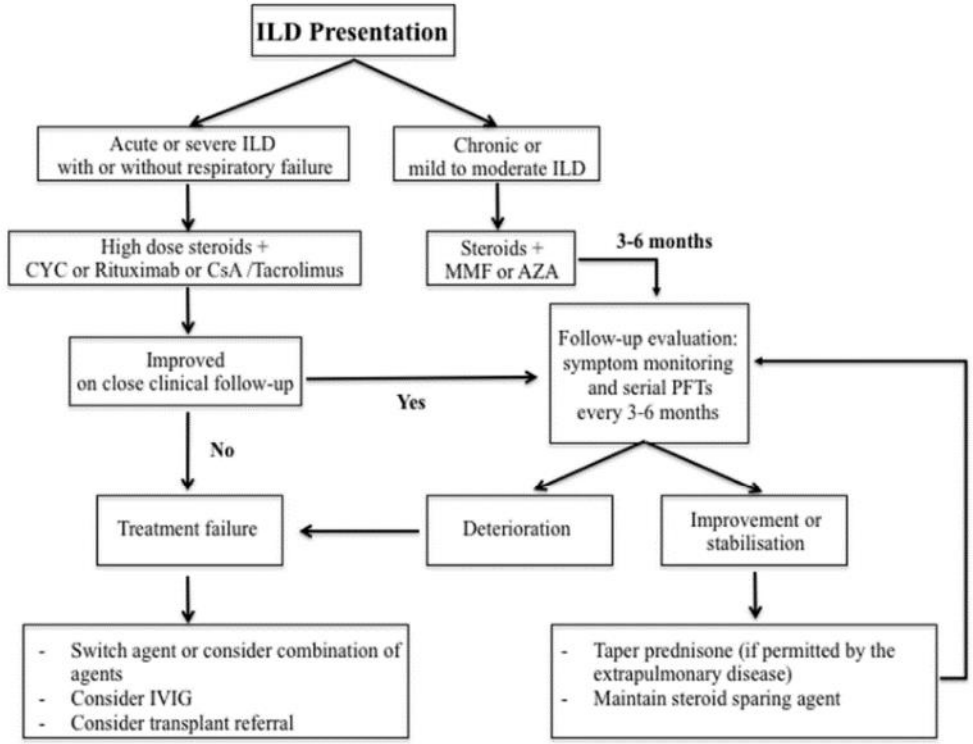
Management of myositis related interstitial lung disease

Julie Morisset, M.D., Cheilonda Johnson, M.D., Eric Rich, M.D., Harold R. Collard, M.D., FCCP, Joyce S. Lee, M.D.

Table 1: Features suggestive of an autoimmune myopathy in a patient with interstitial lung disease

Symptoms	Physical examination findings	Serologic markers	Additional studies
Proximal muscle weakness[1]	Fever[73]	ANA	Elevated CPK levels and/or aldolase[2]
Dysphagia	Mechanic's hands[73] Gottron's papule[1] Dermatomyositis rash (heliotrope rash, v-neck sign)[1]	Myositis-specific antibodies (anti-Jo1, anti-PL7, anti-PL12, anti-EJ, anti-OJ, anti-Mi2, anti-MDA5)[74]	Electromyogram triad of myositis[2]
Raynaud's phenomenon[1,73]	Synovitis	Myositis associated antibodies (Anti-Ro, PM-Scl, anti-Ku)[74]	Muscle edema on MRI
Rash[1]	Objective proximal muscle weakness		Characteristic muscle biopsy[2]
Myalgias [1]	Digital ulcers		
Arthralgias[1]	Puffy fingers/ Sclerodactyly		

Legend: ANA = antinuclear antibodies, CPK= creatine phosphokinase; MRI = magnetic resonance imaging



CHEST (2016), doi: 10.1016/j.chest.2016.04.007.