Actualités Rhumatismes inflammatoires

Denis Mulleman

Rennes 6 octobre 2023

Journée DES

Rennes 6 octobre 2023

Sommaire

- Corticothérapie (2)
- Epidémiologie (3)
- Safety (2)
- Stratégie (2)
- Imagerie (2)

Corticothérapie

Three-month tapering and discontinuation of long- term, low-dose glucocorticoids in senior patients with rheumatoid arthritis is feasible and safe: placebo-controlled double blind tapering after the GLORIA trial

- **Objective** : disease activity, flares and possible adrenal insufficiency after blinded withdrawal of glucocorticoid
- **Method** : GLORIA (Glucocorticoid LOw-dose in RheumatoId Arthritis) trial

- **Results** :

191 patients were eligible; 36 with flare

Flares occurred in **45%** of prednisolone patients compared with **33%** in placebo, relative risk (RR) 1.37 (95% CI 0.95 to 1.98; p=0.12).

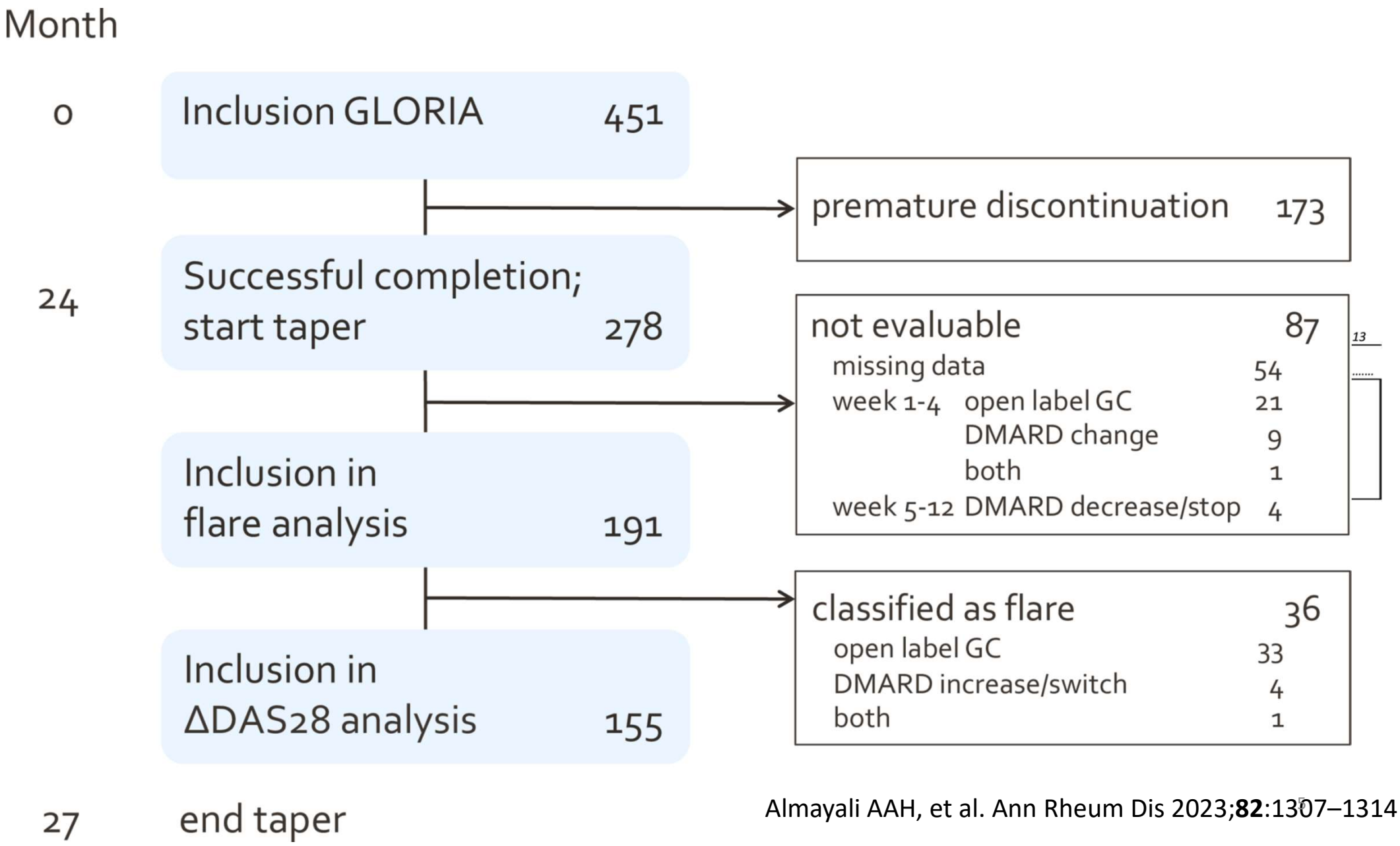
Mean (SD) DAS 28 change at follow-up: **0.2 (1.0)** in the prednisolone group (n=76) vs **0.0 (1.2)** in placebo (n=79).

We found **no evidence for adrenal insufficiency.**

Conclusion/Discussion :

- Tapering prednisolone moderately increases disease activity to the levels of the placebo group (mean still at low disease activity levels) and numerically increases the risk of flare without evidence for adrenal insufficiency. This suggests that withdrawal of low-dose prednisolone is feasible and safe after 2 years of administration.

Almayali AAH, et al. Ann Rheum Dis 2023;**82**:1307–1314



Almayali AAH, et al. Ann Rheum Dis 2023;**82**:1307–1314

Table 2 Effect of tapering on disease activity and patient-reported outcomes

	Prednisolone (n=76)		Placebo (n=79)		
	End of trial	Change after 3 months	End of trial	Change after 3 months	Difference in change*
DAS28 adjusted	2.9 (1.1)	0.2 (1.0)	3.1 (1.0)	0.0 (0.8)	0.16 (0.10) 95% CL –0.06 One-sided p=0.12
DAS components					
ESR	20 (16)	1.9 (11)	25 (20)	–1.5 (13)	2.1
Tender joint count	1.8 (3.5)	0.2 (2.7)	1.8 (4.3)	0.2 (2.0)	0.1
Swollen joint count	0.6 (1.4)	0.4 (1.4)	0.7 (1.7)	0.5 (2.2)	–0.1
Patient global ass.	3.8 (2.6)	0.1 (2.4)	3.7 (2.3)	0.2 (2.3)	0.0
Other core set					
Physician global ass.	2.0 (1.9)	0.3 (1.9)	1.7 (1.4)	0.3 (1.6)	0.1
HAQ	1.0 (0.7)	0.1 (0.4)	1.0 (0.7)	0.0 (0.4)	0.1
CRP (mg/L)	5.4 (9.7)	–0.3 (8.7)	8.1 (11)	–0.6 (7.8)	–1.0
Exploratory					
RAID	3.6 (2.3)	0.1 (1.6)	3.2 (2.1)	0.1 (1.6)	0.2
QALY	0.7 (0.2)	0.0 (0.1)	0.7 (0.2)	0.0 (0.1)	0.0

Change is calculated by subtracting values at the end of the trial from the values at follow-up.
*Adjusted for DAS28 value at final trial visit. Numbers are mean (SD), unless otherwise stated.
CRP, C reactive protein; DAS28, Disease Activity Score 28 joints; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; QALY, quality-adjusted life years measured by the EuroQol 5D (EQ-5D) questionnaire.; RAID, Rheumatoid Arthritis Impact of Disease.

Almayali AAH, et al. Ann Rheum Dis 2023;**82**:1307–1314

Table 3 Patients reporting adrenal insufficiency signs and symptoms

	Prednisolone (n=52)		Placebo (n=64)	
	End of trial	Change after 3 months	End of trial	Change after 3 months
Fatigue (unusual)	11	2	8	1
Appetite loss	4	–2	4	4
Muscle weakness	7	–2	6	–2
Dizziness	3	2	8	3
Stomach pain	3	4	1	2
Muscle pain	17	–5	17	–3
Nausea	3	–2	0	4
Vomiting	0	1	0	1
Diarrhoea	5	–2	1	0
Hypotension*	1	–1	3	–1
Sum, mean (SD) median (q1-q3; max) min-max	1.0 (1.1) 1 (0–2; 4) 0-4	–0.2 (1.3)	0.8 (1.1) 0 (0–1; 6) 0–5	0.1 (1.2)

Sum is the mean sum per patient. Change is calculated by subtracting the values at the end of the trial from the values at follow-up.
*Systolic RR <90 or diastolic RR 60. Numbers represent patients who experience the symptom.
RR, relative risk;

Almayali AAH, et al. Ann Rheum Dis 2023;**82**:1307–1314

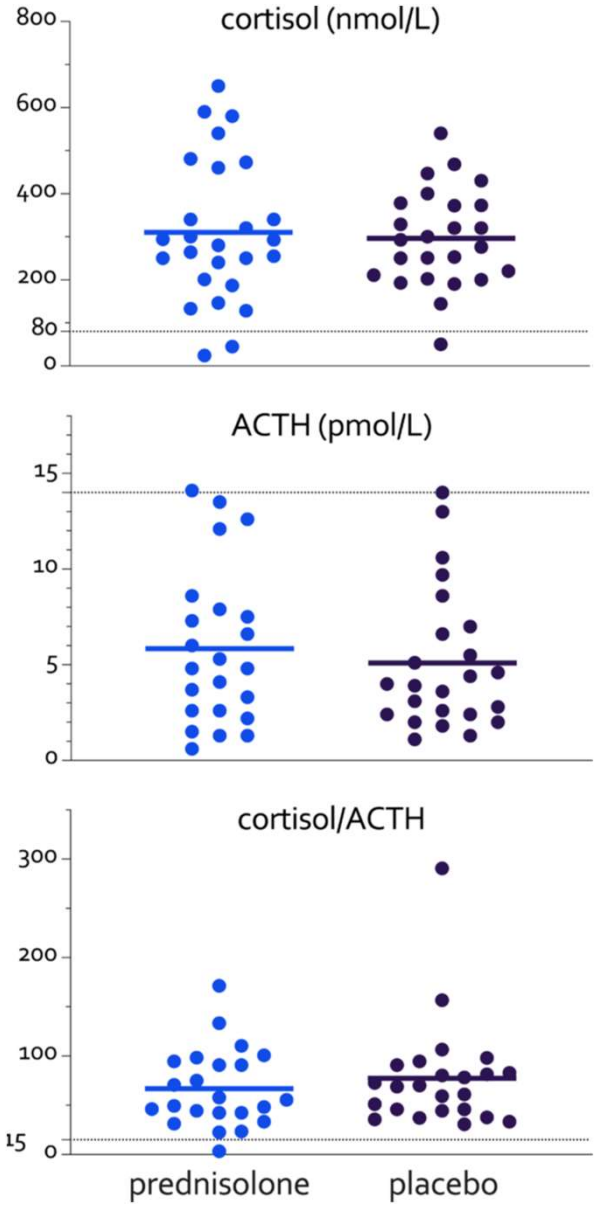


Figure 3 No differences between prednisolone (n=23) and placebo (n=24) patients in spot measurements of cortisol, Adrenocorticotropic Hormone (ACTH) and their ratio. Dotted lines indicate the lower or upper limits of the normal range.

Almayali AAH, et al. Ann Rheum Dis 2023;**82**:1307–1314

Three-month
tapering and discontinuation
of long- term, low-dose
glucocorticoids
in senior patients with
rheumatoid arthritis
is feasible and safe: placebo-
controlled
double blind tapering after the
GLORIA trial

Conclusion

In patients aged 65+ years with RA treated for 2 years with prednisolone 5 mg/day or placebo, **tapering and stopping prednisolone in a period of 3 months moderately increased RA disease activity** to the levels of the placebo group with the mean still at low disease activity levels.

The risk of flares was numerically increased **without any evidence of adrenal insufficiency**, suggesting that withdrawal of low-dose prednisolone in a 3-month schedule is feasible and safe after long-term administration.

Stopping GCs obviously decreases the chance of any GC-related adverse events, and our findings should alleviate fears that low-dose GCs cannot be stopped when given outside a bridging setting.

Almayali AAH, et al. Ann Rheum Dis 2023;**82**:1307–1314

A Phase II randomized controlled trial of oral prednisolone in early diffuse cutaneous systemic sclerosis (PRedSS)

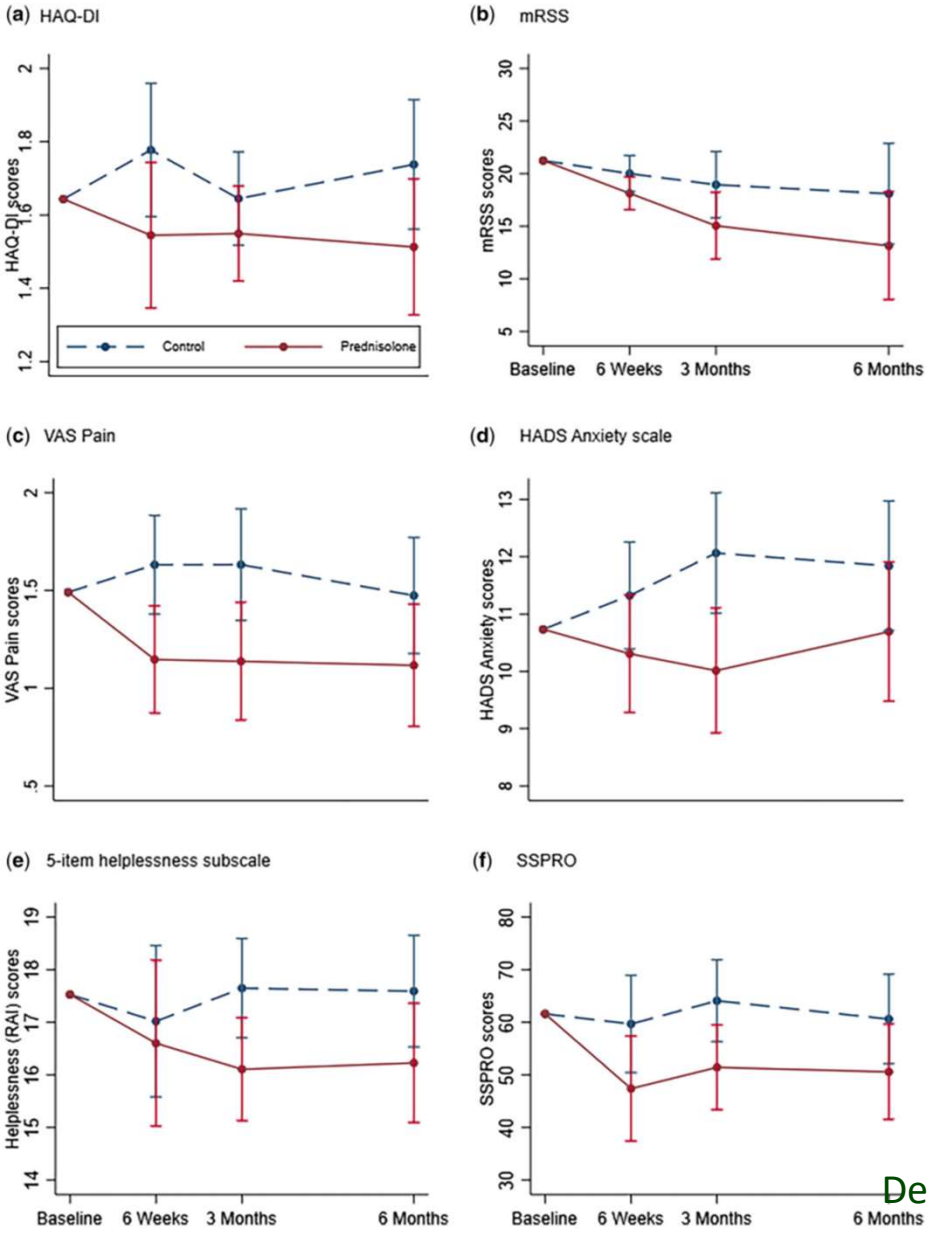
- **Objective** : to examine safety and efficacy of moderate-dose prednisolone in early dcSSc.
- **Method:** Patients were randomized to receive either prednisolone (0.3mg/kg) or matching placebo (or no treatment during open-label) for 6months. Co-primary endpoints were the HAQ Disability Index (HAQ-DI) and modified Rodnan skin score (mRSS) at 3months. Over 20 secondary endpoints included patient reported outcome measures reflecting pain, itch, fatigue, anxiety and depression, and helplessness. Target recruitment was 72 patients..
- **Results** :

- Thirty-five patients were randomized
- Patients in the prednisolone group experienced significantly less pain (0.027), anxiety (0.018) and help lessness (0.040) than control patients at 3 months. There were no renal crises, but sample size was small

- **Conclusion/Discussion :**

- Interpretation must be cautious and results considered inconclusive, indicating the need for a further randomized trial.

Deborah J. Griffiths-Jones et al. Rheumatology, 2023, 62, 3133–3138



Deborah J. Griffiths-Jones et al. Rheumatology, 2023, 62, 3133–3138

Epidémiologie

Country-level socioeconomic status relates geographical latitude to the onset of RA: a worldwide cross-sectional analysis in the METEOR registry

- **Objective** : to what extent differences in patient-specific factors and country-level socioeconomic indicators explain the variability of age of RA at disease onset
- **Method** : METEOR registry
- individual patient characteristics and by country-specific socioeconomic indicators

- **Results** :
- 37 981 patients from 93 hospitals in 17 geographically widespread countries.
- Mean age at diagnosis per country ranged from 39 (Iran) to 55 (Netherlands) years.
- Inclusion of patient-specific factors (eg, gender, anticitrullinated protein antibodies status) in the model augmented the main effect from 0.23 to 0.36 years.

Conclusion/Discussion :

- Patients living closer to the equator get RA at a younger age. This latitude gradient was not explained by individual patient characteristics, but rather by countries' socioeconomic status

Bergstra SA, et al. Ann Rheum Dis 2023;**82**:1018–1024. doi:10.1136/ard-2023-224080

	Spain	US	Portugal	Italy	France	Netherlands	Ireland	UK
Included patients, n	225	1139	4544	5636	210	5094	1367	1510
Included hospitals, n	8	3	18	26	3	8	2	5
Age at diagnosis	49.6 (15.1)	49.7 (13.4)	48.9 (14.6)	46.6 (13.7)	44.7 (12.0)	55.2 (15.2)	44.6 (14.7)	54.3 (14.0)
% female	83	79	81	81	76	67	65	71
Smoking, % ever smoking	44	51	25	98	51	52	80	53
RF % +	85	61	72	79	79	58	52	71
ACPA % +	87	59	69	75	79	54	54	67
Symptom duration at diagnosis median (IQR)	5 (3–12)	5 (1–14)	10 (1–24)	4 (2–12)	5 (1–12)	5 (2–20)	6 (2–12)	9 (4–24)
GDP per capita Intl$	32 219	52 704	26 549	34 220	37 775	46 354	61 378	38 509
Life expectancy	83	79	82	83	83	82	82	82
Gross enrolment ratio secondary school	128	97	118	103	111	132	126	125
Physician density per 1000 inhabitants	3.87	2.47	4.43	4.02	3.24	3.48	2.96	2.83
Health expenditure per capita Intl$	3183	9536	2661	3351	4542	5313	5335	4144

Bergstra SA, et al. Ann Rheum Dis 2023;**82**:1018–1024. doi:10.1136/ard-2023-224080

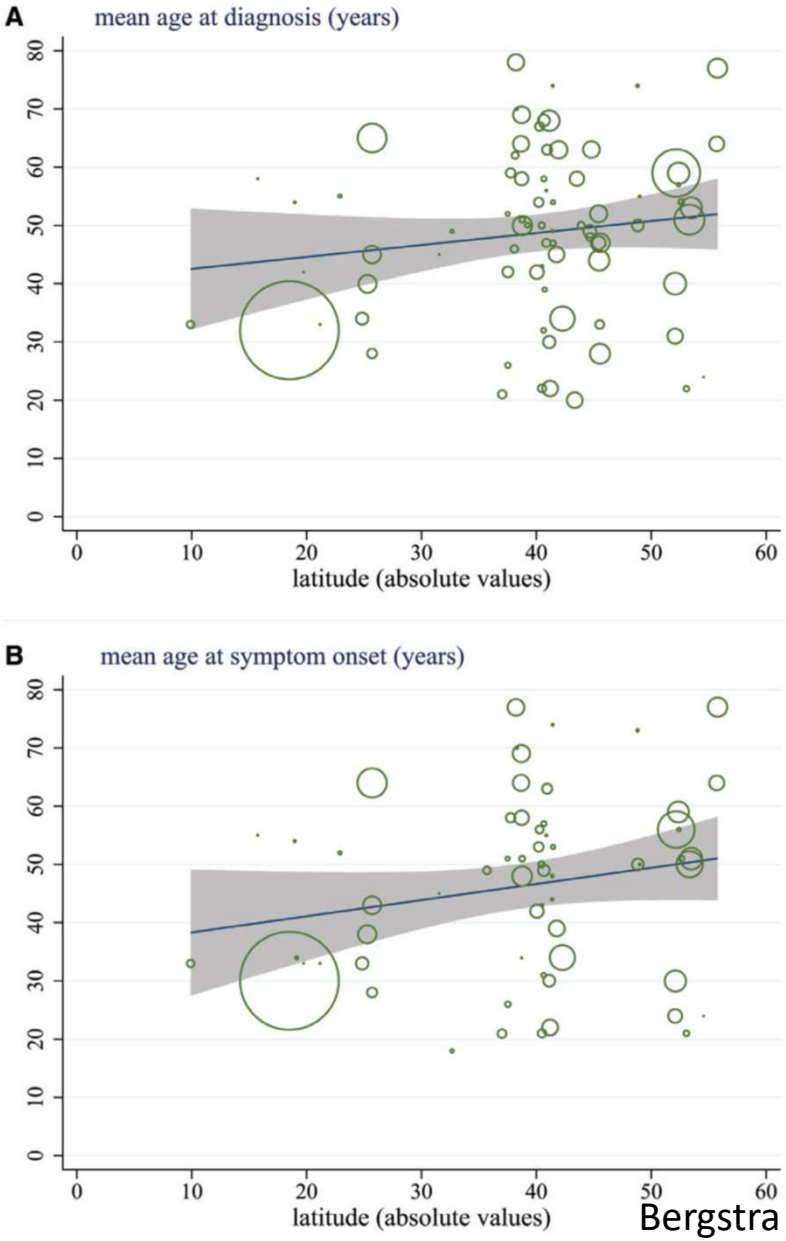


Figure 1 Association between hospital latitude and mean age at diagnosis (A) and mean age at symptom onset (B) per hospital. Green circles indicate the average age per hospital. The circle size indicates the number of patients per hospital. The blue line indicates a fitted linear regression line for the association between latitude and age at diagnosis. The grey zone indicates the 95% CI.

Bergstra SA, et al. Ann Rheum Dis 2023;**82**:1018–1024. doi:10.1136/ard-2023-224080

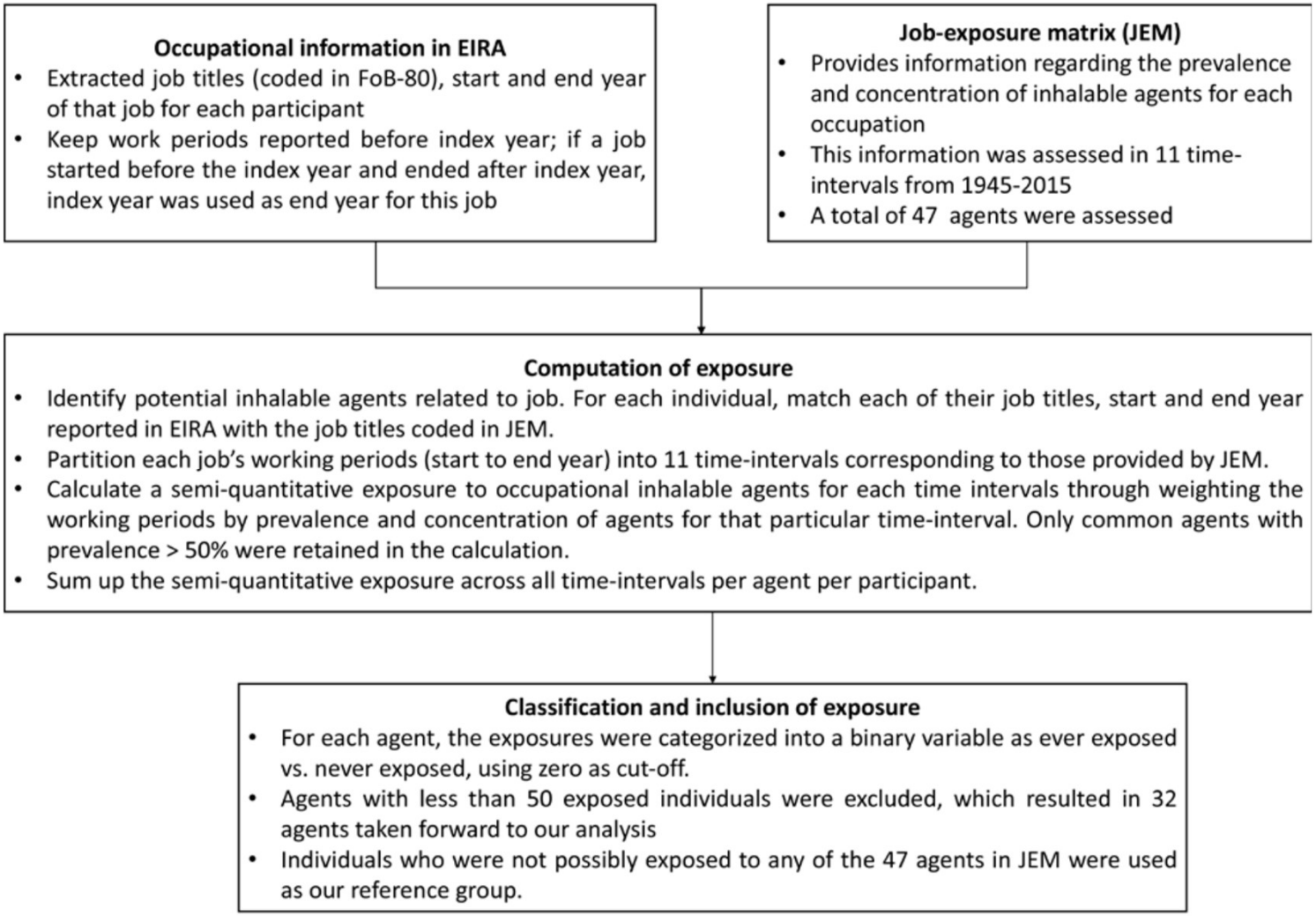
Occupational inhalable agents constitute major risk factors for rheumatoid arthritis, particularly in the context of genetic predisposition and smoking

- **Objective** : To assess the effects of occupational inhalable exposures on rheumatoid arthritis (RA) development
- **Method** : 4033 incident RA cases and 6485 matched controls.
- Swedish national job-exposure matrix
- Exposure to 32 inhalable agents.
- Genetic data were used to define Genetic Risk Score (GRS) or carrying any copy of human leucocyte antigen class II shared epitope (HLA-SE) alleles
- **Results** :

- increased risk for ACPA-positive RA (OR 1.25, 95% CI 1.12 to 1.38). **The risk increased as number of exposed agents increased** (<0.001) or duration of exposure elongated (<0.001).
- **smoking and high GRS, a markedly elevated risk for ACPA-positive RA was observed among the triple-exposed group** compared with those not exposed to any (OR 18.22, 95% CI 11.77 to 28.19).

- **Conclusion/Discussion :**
- Occupational inhalable agents **could act as important environmental triggers in RA development and interact with smoking and RA-risk genes leading to excessive risk for ACPA-positive RA**

Tang B, et al. Ann Rheum Dis 2023;**82**:316–323



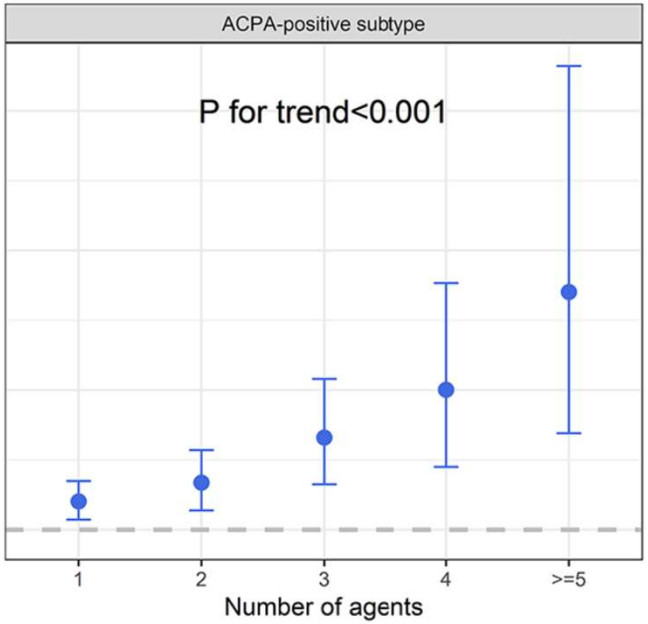
Tang B, et al. Ann Rheum Dis 2023;**82**:316–323

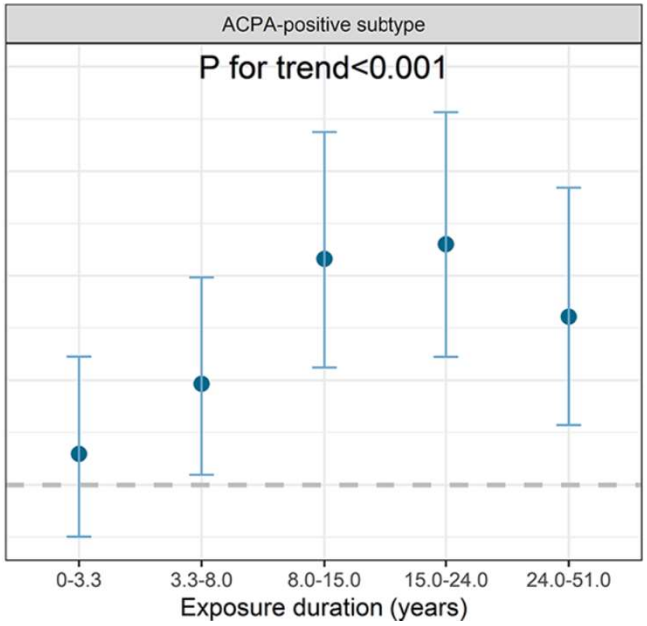
Table 1 Basic characteristics of the study participants

Characteristics	Overall RA cases		Controls	P for ACPA-positive cases versus controls	P for ACPA-negative cases versus controls	P for ACPA-positive versus ACPA-negative cases
	ACPA-positive cases	ACPA-negative cases				
Total N	2642	1391	6485			
Age, mean (SD)	52.93 (12.44)	55.18 (13.07)	53.83 (12.82)	0.002	<0.001	<0.001
Women, N (%)	1908 (72)	946 (68)	4609 (71)	0.28	0.025	0.0058
Education, N (%)						
Primary education	317 (12)	190 (14)	537 (8)	<0.001	<0.001	0.18
Secondary education	1678 (64)	846 (61)	3760 (58)			
University degree	647 (24)	355 (26)	2188 (34)			
Smoking status, N (%)						
Non-smoker	791 (30)	539 (39)	2951 (46)	<0.001	<0.001	<0.001
Ever smoker	1851 (70)	852 (61)	3534 (54)			
Alcohol drinking, N (%)						
Non-drinker	254 (10)	123 (9)	400 6)	<0.001	<0.001	0.46
Ever drinker	2388 (90)	1268 (91)	6085 (94)			
BMI, N (%)						
<20 kg/m^2	188 (7)	85 (6)	378 (6)	0.042	<0.001	0.010
20–25 kg/m^2	1195 (45)	574 (41)	3047 (47)			
>25 kg/m^2	1259 (48)	732 (53)	3060 (47)			
Participants with genetic data, N (%)	2271 (86)	1165 (84)	2838 (44)	<0.001	<0.001	0.068
High genetic predisposition to RA	1949 (86)	670 (58)	1416 (50)	<0.001	<0.001	<0.001
Participants with HLA-DRB1 genotypes available, N (%)	2232 (84)	1171 (84)	2766 (43)	<0.001	<0.001	0.84
With any copy of HLA-SE allele, N (%)	1886 (84)	638 (54)	1451 (52)	<0.001	0.26	<0.001
Ever exposed to any occupational inhalable agents, N (%)	1928 (73)	1007 (72)	4371 (67)	<0.001	<0.001	0.72
Ever exposed to any occupational inhalable agent among women, N (%)	1307 (69)	656 (69)	3003 (65)	0.010	0.015	0.68
Ever exposed to any occupational inhalable agent among men, N (%)	621 (85)	351 (79)	1368 (73)	<0.001	0.012	0.015

ACPA, anticitrullinated protein antibodies; BMI, body mass index; RA, rheumatoid arthritis.

Tang B, et al. Ann Rheum Dis 2023;**82**:316–323





Tang B, et al. Ann Rheum Dis 2023;**82**:316–323

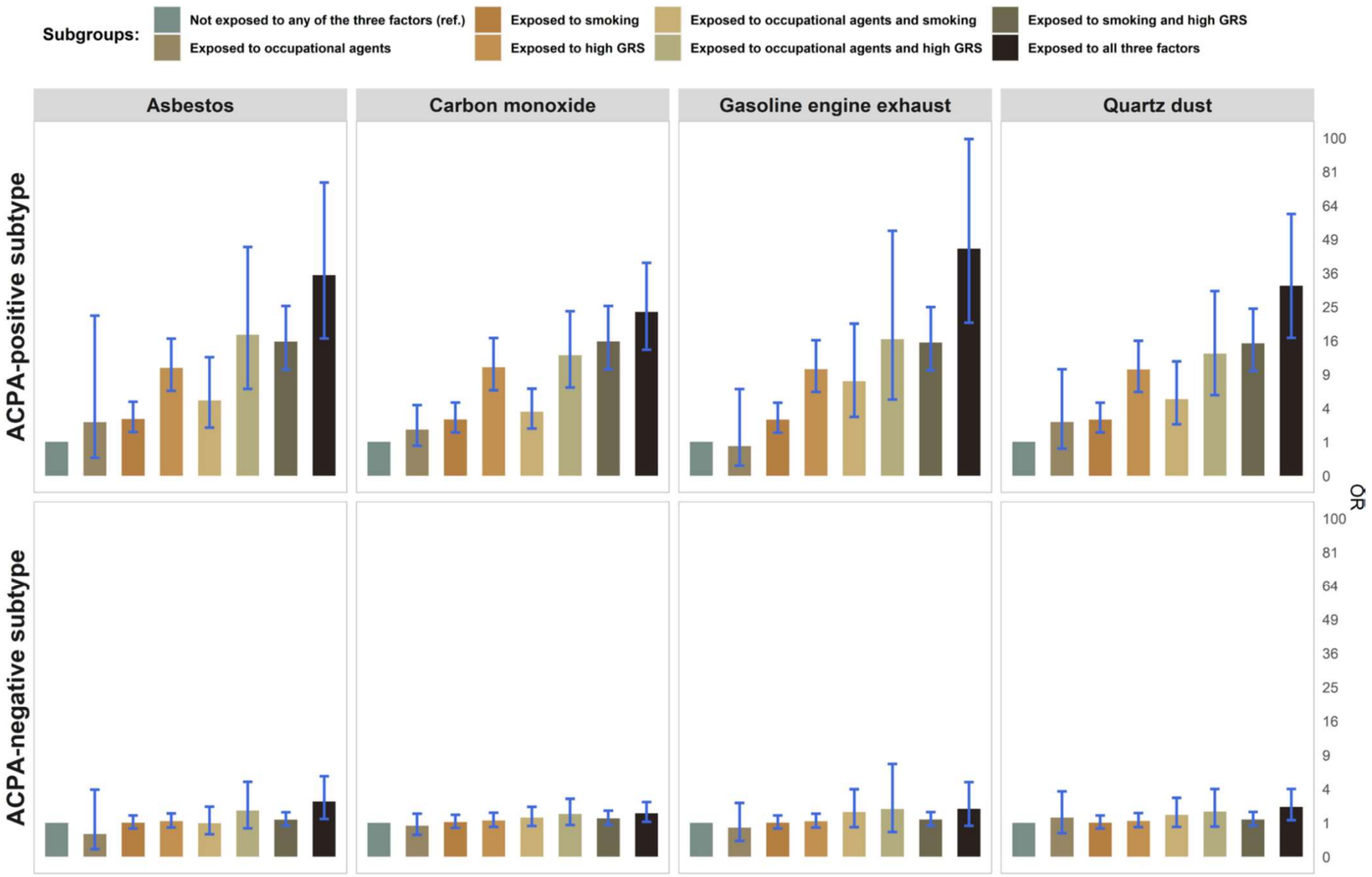


Figure 4 The combined effects of four common inhalable agents, smoking and high genetic risk score with risk for RA. Results are shown for ACPA-positive and ACPA-negative subtypes. Estimates were adjusted for age, sex, residential area, body mass index, levels of education, alcohol drinking and principal components 1–10. ACPA, anticitrullinated protein antibodies; RA, rheumatoid arthritis.

Tang B, et al. Ann Rheum Dis 2023;**82**:316–323

Prevalence and predictors of atlanto-axial subluxation in rheumatoid arthritis after 12-years' follow-up (ESPOIR Cohort)

- **Objective** prevalence and predictors of radiographic aAAS after 12 years' follow-up of patients with early polyarthritis.
- **Method** : early polyarthritis cohort ESPOIR
- atlanto-dental interval>3mm
- All patients still in the cohort after 12 years had dynamic cervical-spine radiographs taken then read by two blinded observers.
- **Results :**

- Of 323 patients followed for 12 years, 15 (**4.6%; 95% CI 2.8, 6.4**) had aAAS

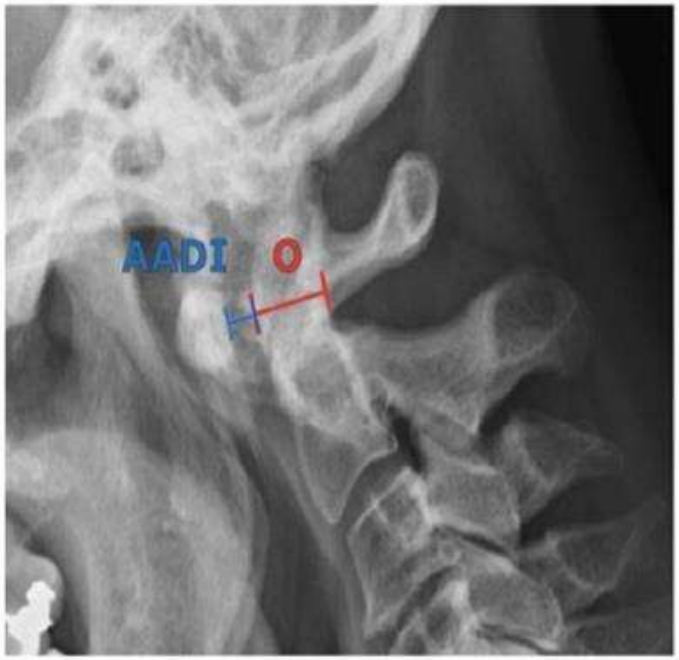
- **CRP and RFs** remained in a model of logistic regression (combination predicted aAAS with a sensitivity of 60% for a specificity of 90%

- **Conclusion/Discussion :**

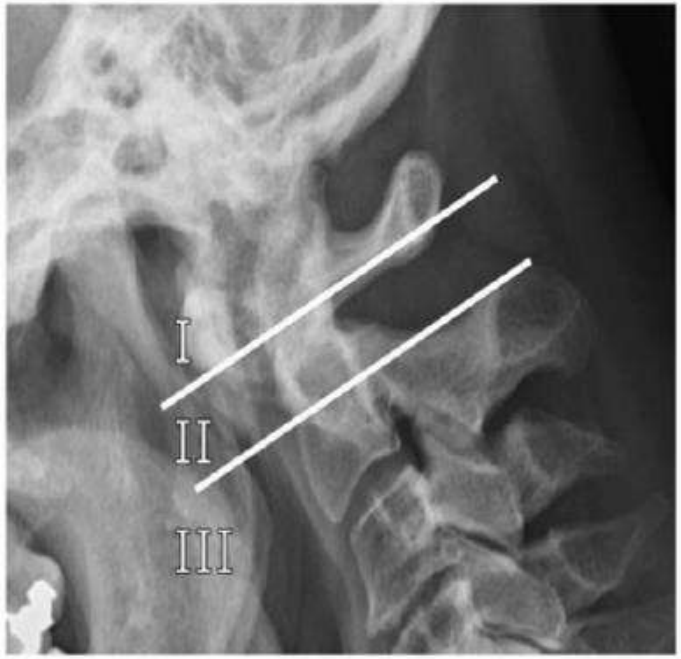
- The prevalence of aAAS after 12 years was 4.6% in the ESPOIR cohort, with no patients having severe aAAS.
- Although some factors were found to be statistically associated to AAS, the event is too rare to allow a clinical relevance.

Aurore Le Quellec et al Rheumatology, 2023, 62, 2692–2699

(a) **Lateral flexion plain radiograph showing the method used for AADI and O measurements**



(b) **Clark station**



The station of the first cervical vertebra is determined by dividing the odontoid process into three equal parts inthe sagittal plane. If the anterior ring of the atlas is level with the middle third (station II) or caudal third (station III) of the odontoid process, basilar invagination is diagnosed

Aurore Le Quellec et al Rheumatology, 2023, 62, 2692–2699

Safety

Impact of NSAIDs on 8-year cumulative incidence of major
cardiovascular events in patients with ankylosing spondylitis: a nationwide study

- **Objective** : incidence of major adverse cardiovascular events (MACEs) in French patients newly benefiting from the French Long-term Illness scheme (LTI) for AS
- **Method** : medico-administrative database SNDS containing data on hospitalization, the LTI, and outpatient care consumption. All French patients newly receiving LTI benefits for AS from 2010
- occurrences of MACEs [stroke and myocardial infarction (MI)] and comorbidities
- **Results** :

Between 2010 and 2013, 22 929 patients were included

NSAIDs [SHR: **0.39 (0.32–0.50),** P<0.001] and anti-TNF [SHR **0.61 (0.46–0.80)**, P<0.001], but not anti-IL17 [**2.10 (0.79–5.57)**] were associated with a lower risk of MACE occurrence.

Conclusion/Discussion : MACE incidence rates at 8 years are low in patients newly benefiting from LTI for AS. Our results support the hypothesis of a **protective role of NSAIDs and anti-TNF in cardiovascular risk** in these patients.

Olivier Fakih et al. Rheumatology, 2023, 62, 3317–3322

Table 1. Characteristics of the study population at baseline and during follow-up ($N = 22\,929$)

Characteristic	At baseline	Occurrence during follow-up
Socio-demographic characteristics		
Age in years, mean (S.D.)	43.0 (13.9)	
Male sex	10 285 (44.9)	
French deprivation index[a], mean (S.D.)	0.01 (0.93)[b]	
Complementary universal health coverage	13 634 (59.5)	
Aid for complementary health coverage	244 (1.1)	
State medical aid	43 (0.2)	
Comorbidities		
–Diabetes	951 (4.2)	821 (3.6)
–Hypertension	3893 (17.0)	2357 (10.3)
–Dyslipidaemia	2269 (10.0)	1145 (5.0)
–Smoking	459 (2.0)	661 (2.9)
–Obesity	117 (0.5)	338 (1.5)
–Chronic kidney disease	57 (0.3)	54 (0.2)
–Atherosclerosis of arteries of extremities	127 (0.6)	126 (0.6)
–Depression	4731 (20.6)	3137 (13.6)
Treatments		
–NSAIDs	19 633 (85.6)	1822 (8.0)
–COX2-selective inhibitors	3518 (15.3)	3035 (13.2)
–Non-selective NSAIDs	19 297 (84.2)	1899 (8.3)
–MTX	930 (4.1)	3465 (15.1)
–LEF	112 (0.5)	366 (1.6)
–SSZ	1760 (7.7)	2079 (9.1)
–Anti-TNF	1344 (5.9)	9456 (41.2)
–Anti-IL17	0	1095 (4.8)

Values are *n* (%) unless otherwise stated.
[a] The index value increases as social deprivation increases.
[b] A total of 582 study participants had missing data for the French deprivation index.
There were no missing data for other variables.

Table 2. Univariate analysis showing the levels of association between comorbidities with MACEs and treatments with MACEs

Covariate	Subhazard ratio	95% CI
Age	1.07***	1.06, 1.07
Male sex	1.61***	1.31, 2.00
Free complementary universal health coverage (CMU-C)	1.19	0.95, 1.48
Aid for complementary health coverage (ACS)	1.81	0.81, 4.07
Diabetes	2.21***	1.63, 3.00
Dyslipidaemia	3.67***	2.96, 4.57
Hypertension	3.74***	3.02, 4.63
Smoking	0.79	0.45, 1.37
Obesity	0.58	0.22, 1.56
Chronic kidney disease	1.18	0.29, 4.72
Atherosclerosis of arteries of extremities	4.64***	2.87, 7.49
Depression	1.01	0.81, 1.26
NSAIDs	0.35***	0.28, 0.43
COX2-selective inhibitors	0.56*	0.36, 0.89
Non-selective NSAIDs	0.38***	0.30, 0.47
MTX	0.71	0.45, 1.13
LEF	2.27	0.85, 6.07
SSZ	1.03	0.63, 1.67
Anti-TNF	0.59***	0.45, 0.78
Anti-IL17	1.92	0.72, 5.15

Bolded data correspond to covariates statistically significantly associated with the occurrence of MACEs.
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, otherwise non-significant.

Olivier Fakih et al. Rheumatology, 2023, 62, 3317–3322

Is methotrexate safe for men with an immune-mediated inflammatory disease and an active desire
to become a father? Results of a prospective cohort study (iFAME-MTX)

- **Objective** : evaluate the testicular toxicity profile of MTX

- **Method** : two semen samples (a pre-exposure and a post-exposure
- sample after 13 weeks
- Conventional semen analyses, male reproductive endocrine axis and sDFI were compared between groups. FPGS enzymatic activity and
- MTX-PG1-5 concentrations were determined by mass spectrometry analytical methods.
- **Results** :
- The pre-exposure and postexposure semen parameters of MTX-starters were not statistically significant different. Compared with healthy controls, the conventional semen parameters and the sDFI of MTX-starters were not statistically significant different.
- Marginal accumulation of MTX-PGs in spermatozoa
- **Conclusion/Discussion :**
- Treatment with MTX is not associated with testicular toxicity and can be safely started or continued in men and with a wish to become a father

Perez-Garcia LF, et al. Ann Rheum Dis 2023;**82**:1068–1075.

Table 2 Conventional semen parameters and sperm morphology

	MTX-naïve Pre-exposure (n=20)	MTX-naïve Post-exposure (n=18)	Healthy controls (n=25)	MTX chronic* (n=5)	P value
Conventional semen parameters					
Sperm concentration x10^6/mL, median (IQR)	57.0 (35.0–90.5)	54.0 (41.0–82.0)	60.0 (37.0–111.0)	37.0 (32.0–59.9)	NS
Progressive motility* %, mean (95% CI)	63.2 (55.4 to 70.9)	60.1 (49.5 to 70.6)	56.9 (51.1 to 62.8)	50.4 (34.8 to 65.9)	NS
Semen volume mL, median (IQR)	2.4 (1.6–3.2)	3.0 (1.5–3.2)	3.0 (2.0–4.0)	2.0 (1.6–2.4)	NS
Sperm morphology evaluation					
Normal morphology %, mean (95% CI)	6.4 (4.5 to 8.3)	7.1 (5.6 to 8.4)	6.3 (4.7 to 7.9)	5.9 (2.6 to 9.1)	NS
Teratozoospermia index, mean (95% CI)	1.2 (1.2 to 1.3)	1.3 (1.2 to 1.4)	1.2 (1.2 to 1.3)	1.2 (1.1 to 1.4)	NS
Excess residual cytoplasm, median (IQR)	2.0 (0.7–4.3)	2.0 (1.0–4.5)	2.0 (1.0–4.0)	2.0 (1.0–4.0)	NS
Abnormalities in head (%), mean (95% CI)	92.8 (90.8 to 94.7)	93.0 (91.2 to 94.6)	92.7 (91.0 to 94.3)	92.3 (88.0 to 96.5)	NS
Abnormalities in middle piece (%), mean (95% CI)	19.2 (14.2 to 24.1)	24.5 (18.6 to 30.2)	19.9 (15.3 to 24.5)	22.9 (5.7 to 40.0)	NS
Abnormalities in tail (%), mean (95% CI)	7.1 (3.8 to 10.5)	7.3 (3.7 to 11.1)	6.6 (3.9 to 9.3)	4.6 (1.4 to 7.7)	NS

*Presented only for descriptive purposes, no statistical analyses were conducted.
MTX, methotrexate.

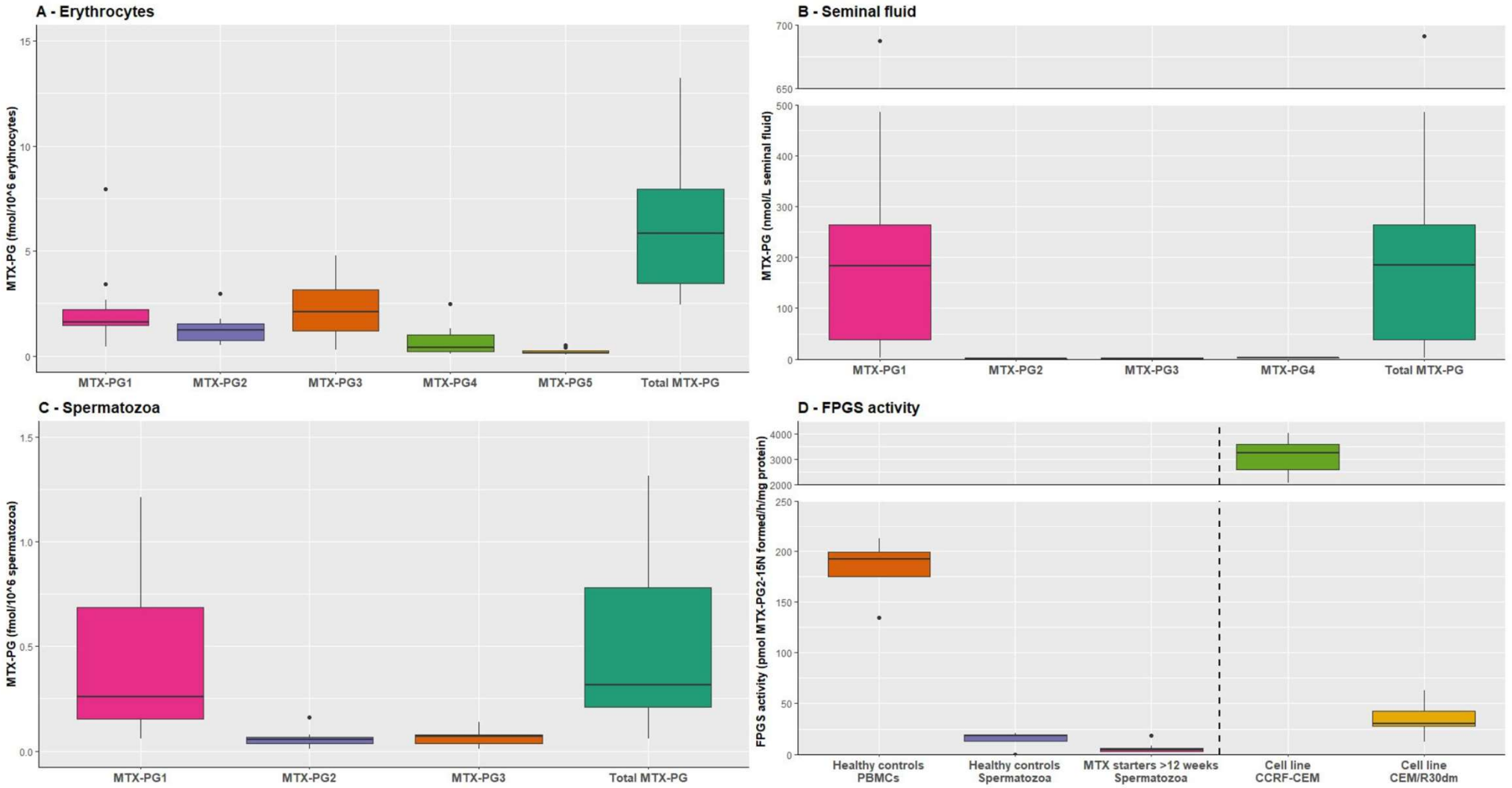
Perez-Garcia LF, et al. Ann Rheum Dis 2023;**82**:1068–1075.

Table 4 Male reproductive endocrine axis

	MTX-naïve Pre-exposure (n=20)	MTX-naïve Post-exposure (n=18)	Healthy controls (n=25)	MTX chronic‡ (n=5)	P value
Testosterone (nmol/L) median (IQR)	14.6 (11.3–16.2)	13.4 (12.0–15.6)	14.1 (12.8–16.7)	16.3 (16.3–17.1)	NS
SHBG (nmol/L) median (IQR)	26.6 (22.6–34.6)	28.8 (22.5–34.6)	32.6 (25.7–41.9)	35.4 (34.1–38.7)	NS
LH (U/L) median (IQR)	3.1 (2.3–3.9)	2.7 (2.2–3.2)	2.9 (2.2–3.4)	4.10 (4.0–4.1)	NS
FSH (U/L) median (IQR)	4.6 (3.5–5.3)	4.2 (3.2–5.0)	3.7 (3.0–4.5)	4.1 (4.0–4.1)	NS
Inhibin B (ng/L) median (IQR)	132.5 (101.5–179.5)	123.0 (116.0–179.0)	189.0 (170.0–236.0)	92.2 (87.0–203.0)	* p=<0.001 p=<0.001

*Statistically significant difference between pre-exposure and healthy controls.
†Statistically significant difference between post-exposure and healthy controls.
‡Presented only for descriptive purposes, no statistical analyses were conducted.
FSH, follicle stimulating hormone; LH, luteinising hormone; MTX, methotrexate; SHBG, sex hormone binding globulin.

Perez-Garcia LF, et al. Ann Rheum Dis 2023;**82**:1068–1075.



Perez-Garcia LF, et al. Ann Rheum Dis 2023;**82**:1068–1075.

Is methotrexate safe for men with an immune-mediated inflammatory disease and an active desire
to become a father? Results of a prospective cohort study (iFAME-MTX)

Methotrexate is not associated with testicular toxicity in men diagnosed with an IMID. It can also be concluded that the concentration of intracellular Methotrexate-PG in seminal fluid and spermatozoa is very low. Therefore, therapy with Methotrexate can be safely started or continued in men diagnosed with an IMID and with an active wish to become a father.

Perez-Garcia LF, et al. Ann Rheum Dis 2023;**82**:1068–1075.

Identification of two tofacitinib subpopulations with
different relative risk versus TNF inhibitors: an analysis of the open label, randomised controlled study ORAL Surveillance

- **Objective** : Determine whether the Bone Mineral Density (BMD) response to Teriparatide might be influenced by genetic factors
- **Method** : Multicenter (3 referral centres : Edinburgh (UK), Aarhus (Denmark) and Ljubljana (Slovenia)) association study in 437 patients with osteoporosis.

- BMD was measured at the lumbar spine (L1–L4), total hip and femoral neck prior to starting TPTD therapy and at the end of treatment.
- Clinical and demographic data were obtained from the participants' medical records.

- **Results** :

- Allelic variation at rs6430612 on chromosome 2 was significantly associated with the response of spine BMD to Teriparatide (p = 9.2x10*-9) ; Individuals homozygous for the A allele at rs6430612 had a 16% increase in spine BMD compared with a 7.3% for homozygotes for the G allele, with intermediate responses in heterozygotes. Response of femoral neck and total hip BMD to TPTD was also significantly associated with rs6430612 allelic variants

- Variants at rs73056959 were not significantly associated with change in lumbar spine BMD (p=0.20), but were significantly associated with change in both femoral neck BMD (p=4×10−5) and total hip BMD (p=3.3×10−4).

- **Conclusion/Discussion :**

- Genetic factors are associated with a response to Teriparatide at the lumbar spine and hip with a magnitude of effect that is clinically relevant.

- But this study is an association study : we can't make full conclusion out of this. Further studies are required to identify the causal genetic variants and underlying mechanisms as well as to explore how genetic testing for these variants might be implemented in clinical practice.

Genome-wide association study identifies genetic variants which predict the response of bone mineral density to teriparatide therapy. Nerea Alonso ,1,2 Omar M E Albagha,1,3 Asim Azfer,1 Beatriz Larraz-Prieto,1 Kathryn Berg,1 Philip L Riches,1,4 Barbara Ostanek,5 Tomaz Kocjan,6,7 Janja Marc,5 Bente L Langdahl,8 Stuart H Ralston

Stratégie

Rituximab versus azathioprine for maintenance of remission for patients with ANCA-associated vasculitis and relapsing disease: an international randomised controlled trial

- **Objective** : Determine whether the Bone Mineral Density (BMD) response to Teriparatide might be influenced by genetic factors
- **Method** : Multicenter (3 referral centres : Edinburgh (UK), Aarhus (Denmark) and Ljubljana (Slovenia)) association study in 437 patients with osteoporosis.

- BMD was measured at the lumbar spine (L1–L4), total hip and femoral neck prior to starting TPTD therapy and at the end of treatment.
- Clinical and demographic data were obtained from the participants' medical records.

- **Results** :

- **Allelic variation at rs6430612 on chromosome 2** was significantly associated with the response of spine BMD to Teriparatide (p = 9.2x10*-9) ; Individuals homozygous for the A allele at rs6430612 had a 16% increase in spine BMD compared with a 7.3% for homozygotes for the G allele, with intermediate responses in heterozygotes. Response of femoral neck and total hip BMD to TPTD was also significantly associated with rs6430612 allelic variants

- Variants at rs73056959 were not significantly associated with change in lumbar spine BMD (p=0.20), but were significantly associated with change in both femoral neck BMD (p=4×10−5) and total hip BMD (p=3.3×10−4).

- **Conclusion/Discussion :**

- Genetic factors are associated with a response to Teriparatide at the lumbar spine and hip with a magnitude of effect that is clinically relevant.

- But this study is an association study : we can't make full conclusion out of this. Further studies are required to identify the causal genetic variants and underlying mechanisms as well as to explore how genetic testing for these variants might be implemented in clinical practice.

Genome-wide association study identifies genetic variants which predict the response of bone mineral density to teriparatide therapy. Nerea Alonso ,1,2 Omar M E Albagha,1,3 Asim Azfer,1 Beatriz Larraz-Prieto,1 Kathryn Berg,1 Philip L Riches,1,4 Barbara Ostanek,5 Tomaz Kocjan,6,7 Janja Marc,5 Bente L Langdahl,8 Stuart H Ralston

Comparative safety and effectiveness of TNF inhibitors, IL6 inhibitors and methotrexate for the treatment of immune checkpoint inhibitor-associated arthritis

- **Objective** : To compare the safety and effectiveness of biologic and conventional disease-modifying antirheumatic drugs (DMARDs) for immune checkpoint inhibitor-associated inflammatory arthritis (ICI-IA).
- **Methods** Retrospective multicentre observational , ICI-IA patients treated with a tumour necrosis factor inhibitor (TNFi), interleukin-6 receptor inhibitor (IL6Ri) and/ or methotrexate (MTX)
- **Results** :
- **37% of patients with ICI-IA required treatment** with a tumour necrosis factor inhibitor (TNFi), interleukin-6 receptor inhibitor (IL6Ri) and/or methotrexate (MTX).Total 147 (100%) TNFi 33 (22%) IL6R 42 (29%) MTX 72 (49%)
- Time to cancer progression was significantly **shorter for TNFi compared with MTX** (HR 3.27 (95% CI 1.21 to 8.84, p=0.019)) while the result for IL6Ri was HR 2.37 (95% CI 0.94 to 5.98, p=0.055).
- Time to arthritis control was **faster for TNFi compared with MTX** (HR 1.91 (95% CI 1.06 to 3.45, p=0.032)) while the result for IL6Ri was HR 1.66 (95% CI 0.93 to 2.97, p=0.089).
- **Conclusion/Discussion :**

The treatment of ICI-IA with a biologic DMARD is associated with more rapid arthritis control than with MTX, but may be associated with a shorter time to cancer progression.

Bass AR, et al. Ann Rheum Dis 2023;**82**:920–926.

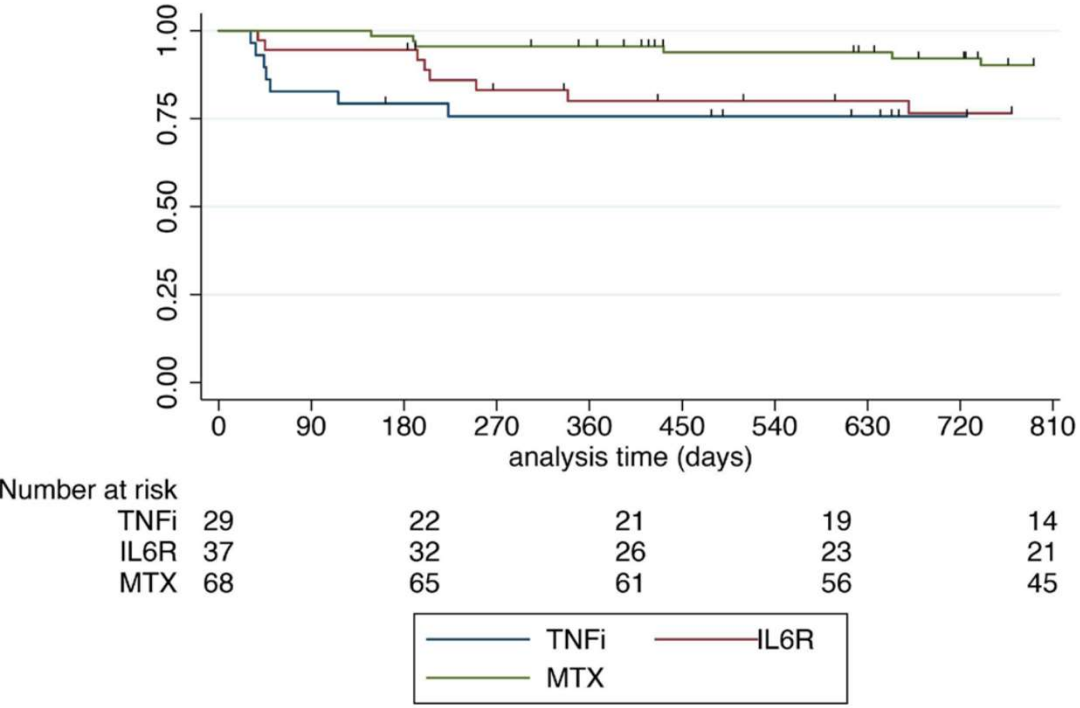


Figure 1 Kaplan-Meier survival estimates: time to cancer progression from immune checkpoint inhibitor initiation. Patients whose cancer progressed prior to disease-modifying antirheumatic drug (DMARD) initiation were excluded. IL6R, interleukin-6 receptor; MTX, methotrexate; TNFi, tumour necrosis factor inhibitor.

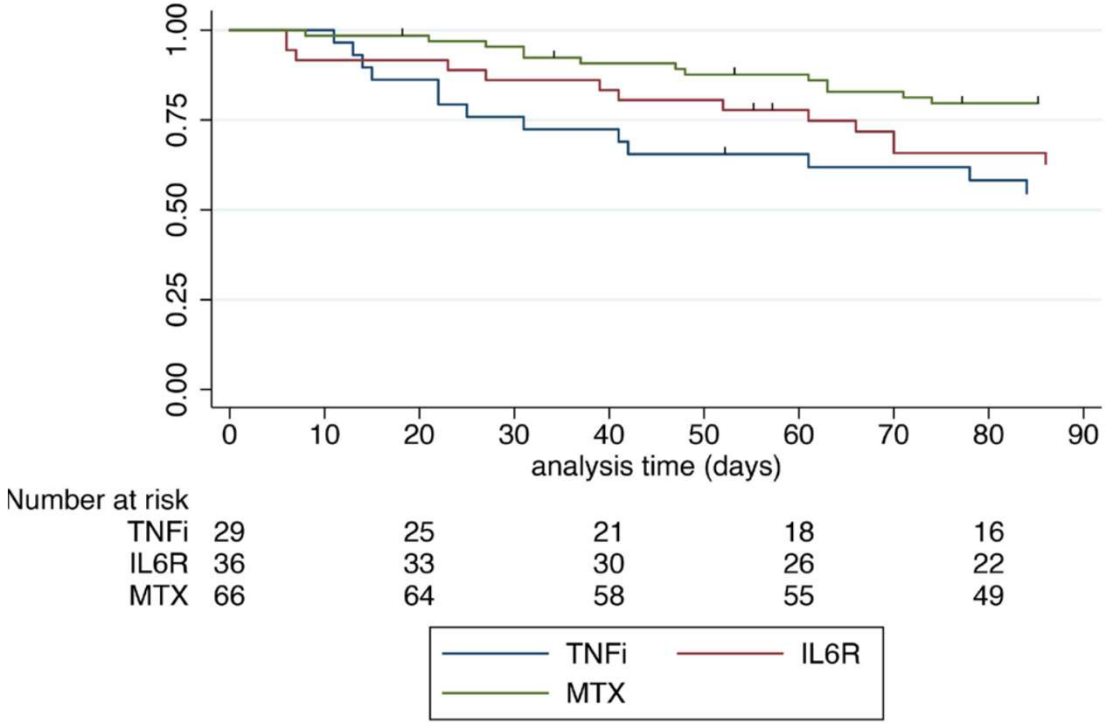


Figure 4 Kaplan-Meier survival estimates: time to arthritis control from disease-modifying antirheumatic drug initiation within the first 90 days. IL6R, interleukin-6 receptor; MTX, methotrexate; TNFi, tumour necrosis factor inhibitor.

Bass AR, et al. Ann Rheum Dis 2023;**82**:920–926.

Comparative safety and effectiveness of TNF inhibitors, IL6 inhibitors and methotrexate for the treatment of immune checkpoint inhibitor-associated arthritis

- Conclusion

MTX should be considered over a bDMARD in patients with chronic steroid-dependent ICI-IA, when disease activity allows.

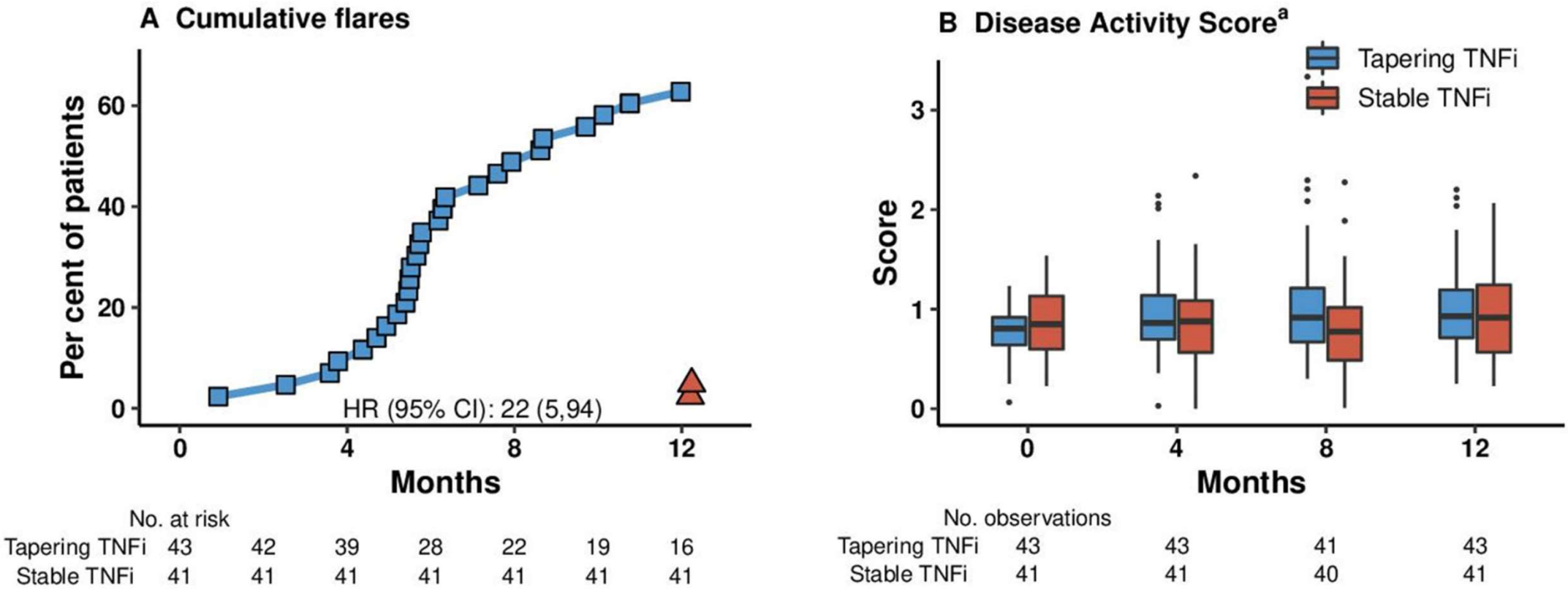
Some patients with severe ICI-IA may require a biologic DMARD rather than MTX to achieve rapid arthritis control and avoid the prolonged use of high-dosesteroids.

Genome-wide association study identifies genetic variants which predict the response of bone mineral density to teriparatide therapy. Nerea Alonso ,1,2 Omar M E Albagha,1,3 Asim Azfer,1 Beatriz Larraz-Prieto,1 Kathryn Berg,1 Philip L Riches,1,4 Barbara Ostanek,5 Tomaz Kocjan,6,7 Janja Marc,5 Bente L Langdahl,8 Stuart H Ralston

Effect of tapered versus stable treatment with tumour necrosis factor inhibitors on disease flares in patients with rheumatoid arthritis in remission: a randomised, open label, non-inferiority trial

- **Objective** : to assess the effect of tapering TNFi to withdrawal compared with stable treatment on the risk of disease activity flares in patients with RA in remission ≥1 year
- **Method** : randomised, open-label, non-inferiority trial was undertaken at nine Norwegian rheumatology departments. Patients with RA in remission ≥12 months
- Tapering to discontinuation of TNFi or stable TNFi..
- Disease flare during the 12-month study period
- **Results** :
- Eighty-four patients were included in the per-protocol population.
- In the tapering TNFi group, 27/43 (**63%**) experienced a flare during 12 months, compared with 2/41 (**5%**) in the stable TNFi group;
- **Conclusion/Discussion :**
- patients with RA in remission for more than 1 year while using TNFi, an **increase in flare rate was reported in those who tapered TNFi to discontinuation.**
- However, **most regained remission after reinstatement of full-dose treatment**.

Lillegraven S, et al. Ann Rheum Dis 2023;**0**:1–10.



Lillegraven S, et al. Ann Rheum Dis 2023;**0**:1–10.

Cost–utility analysis of tapering strategies of biologicals in rheumatoid arthritis patients in the Netherlands

- **Objective** :To evaluated the sensitivity to change and discriminative abilities of vascular US scores in disease monitoring in new-onset cranial and large-vessel (LV) GCA patients.
- Methods: Baseline and follow-up (8 weeks, 24 weeks and 15 months) US of temporal arteries (TA), carotid and axillary arteries (LV) included assessment of halo and measurement of the intima media complex (IMC).
- The provisional OMERACT US score, OGUS, was obtained, taking the average of temporal arteries and axillary arteries IMCs divided by their normal cut-off values.
- Results: Baseline US was positive in 44/47 patients (72% TA, 72% LV). Sensitivity to change of all composite US scores containing TAs was evident by week 8 onward.
- The OGUS showed a large magnitude of change
- Conclusions: The OGUS is suggested as an outcome measurement for the assessment of treatment response in clinical trials.

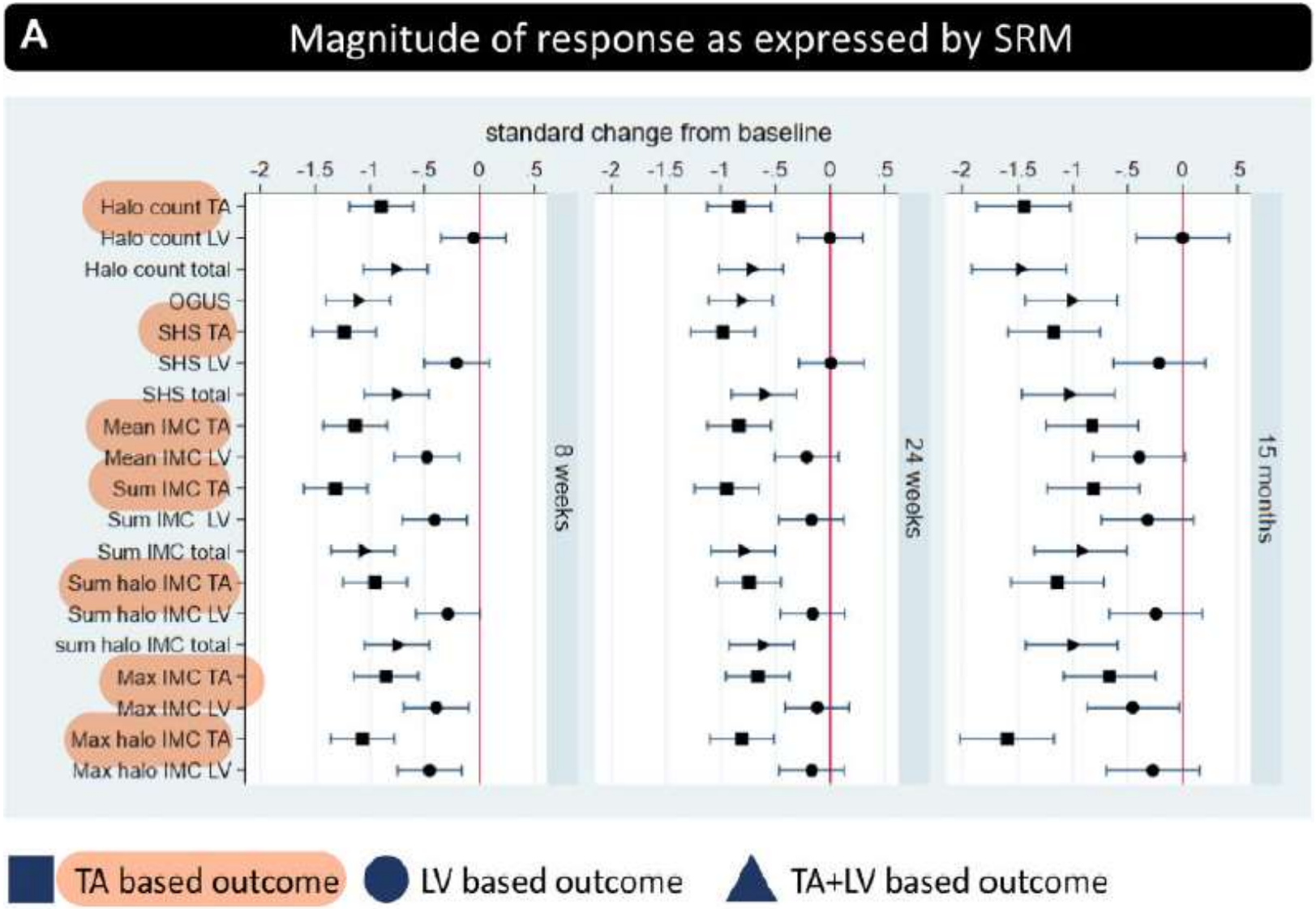
Berit Dalsgaard Nielsen et al. Rheumatology, 2023, 62, 3084–3094

Imagerie

Ultrasonography in the assessment of disease activity in cranial and large-vessel giant cell arteritis: a prospective follow-up study

- **Objective** :To evaluated the sensitivity to change and discriminative abilities of vascular US scores in disease monitoring in new-onset cranial and large-vessel (LV) GCA patients.
- Methods: Baseline and follow-up (**8 weeks, 24 weeks and 15 months**) US of temporal arteries (TA), carotid and axillary arteries (LV) included assessment of halo and measurement of the intima media complex (IMC).
- The provisional OMERACT US score, OGUS, was obtained, taking the average of temporal arteries and axillary arteries IMCs divided by their normal cut-off values.
- Results: Baseline US was positive in 44/47 patients (72% TA, 72% LV). **Sensitivity to change of all composite US scores containing TAs was evident by week 8 onward.**
- The OGUS showed a large magnitude of change
- Conclusions: The OGUS is suggested as an outcome measurement for the assessment of treatment response in clinical trials.

Berit Dalsgaard Nielsen et al. Rheumatology, 2023, 62, 3084–3094



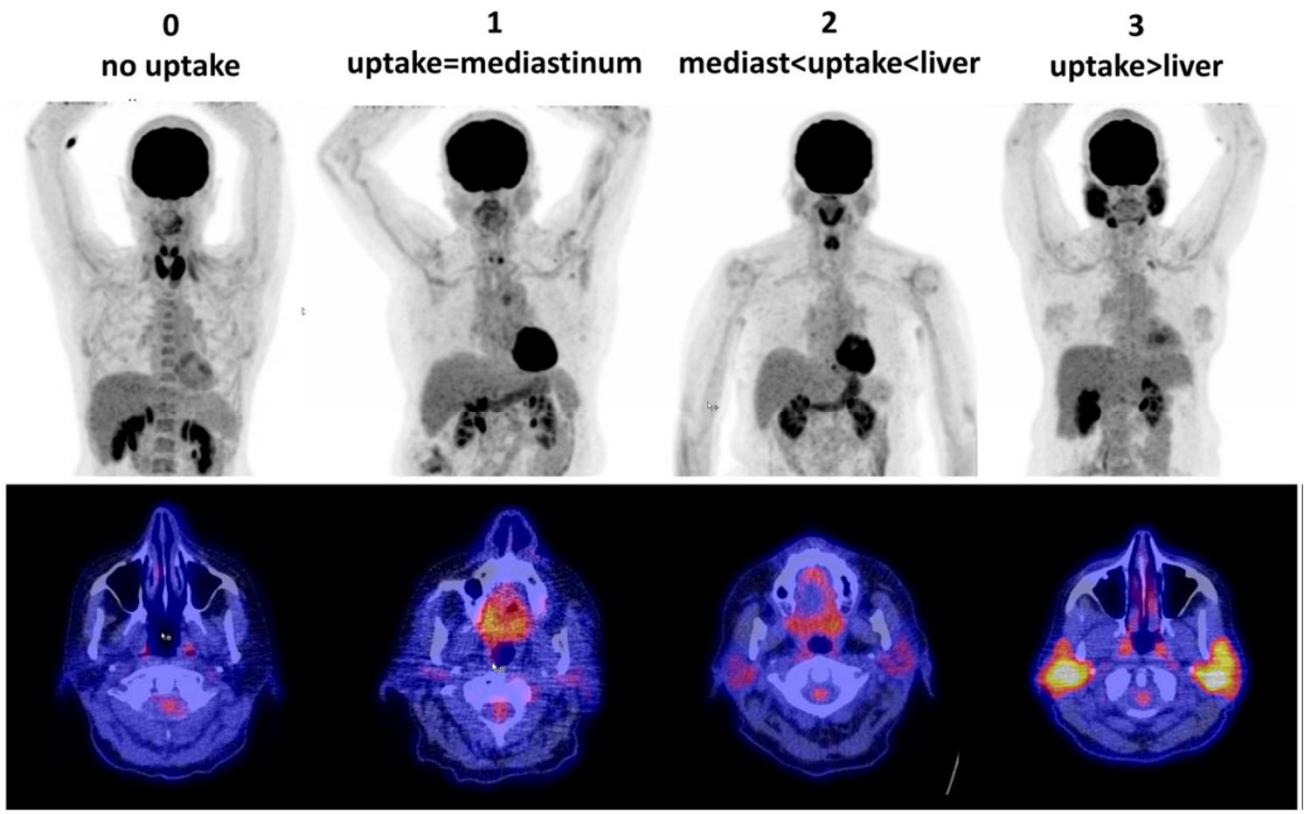
SRM= Standard response mean

Berit Dalsgaard Nielsen et al. Rheumatology, 2023, 62, 3084–3094

FDG-PET/CT discriminates between patients with and without lymphomas in primary Sjögren's syndrome

- **Objectives**: To assess the usefulness of PET/CT to discriminate between primary SS (pSS) patients with and without lymphomas
- **Methods**: visual evaluation and quantitative analysis by SUV of salivary and lacrimal glands and systemic regions. Receiver operating characteristic curve analyses to discriminate between lymphoma and non-lymphoma.
- **Results**: 70 patients, 26 were diagnosed with a pSS-associated lymphoma. Lymphoma patients showed higher FDG uptake in the parotid and submandibular glands, and more frequently showed presence of nodular lung lesions, compared with non-lymphoma patients.
- **Conclusions**: FDG-PET/CT can assist in excluding pSS-associated lymphomas in patients without PET abnormalities, possibly leading to a decrease of invasive biopsies in suspected lymphoma patients.

Martha S. van Ginkel et al. Rheumatology, 2023, 62, 3323–3331



Martha S. van Ginkel et al. Rheumatology, 2023, 62, 3323–3331

The highest SUVmax of the parotid glands to predict lymphoma diagnosis (any lymphoma type, at any location) was good, with an AUC of 0.83

Table 3. Sensitivity and specificity of PET parameters to discriminate between pSS patients with and without lymphoma

	Number of patients	Sensitivity	Specificity	PPV	NPV
Separate items					
Par SUVmax > 3.1	N = 69	76% (19/25)	82% (36/44)	70% (19/27)	86% (36/42)
Subm SUVmax > 2.9	N = 67	67% (16/24)	84% (36/43)	70% (16/23)	82% (36/44)
Presence of nodular lung lesions	N = 70	31% (8/26)	93% (41/44)	73% (8/11)	70% (41/59)
Combination scores					
1 out of 3 present	N = 69	92% (24/26)	67% (29/43)	63% (24/38)	94% (29/31)
2 out of 3 present	N = 68	75% (18/24)	91% (40/44)	82% (18/22)	87% (40/46)

pSS: primary SS; PPV: positive predictive value; NPV: negative predictive value; Par: parotid gland; Subm: submandibular gland; SUVmax: maximum standardized uptake value.

Martha S. van Ginkel et al. Rheumatology, 2023, 62, 3323–3331

Merci de votre attention