

Rheumatologie aus wissenschaftlicher Sicht – Fallbesprechung

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Anamnese

78-jährige Pat. seit 3-4 Tagen Krankheitsgefühl, erhöhte Temperatur, Kopfschmerzen,

z.T. Doppelbilder

Myalgien Oberarme, Oberschenkel, HWS-bereich

Kontrolle bei Augenärztin (Wahlärztin) wg. Glaukom

Verdachtsdiagnose? Weiteres Procedere?

Untersuchungsergebnisse

Status: unauffällig

Rheumastatus: „nur“ Fingerpolyarthrose, Abduktion bd. Schultergl. bis 80°

C/P: unauffällig, kein Infiltrat

HÄMATOLOGIE

Blutbild:

Leukozyten	6.3	G/l	4.0-10.0	
Thrombozyten	↑ 382	G/l	150-350	
Erythrozyten	4.5	T/l	3.8-5.2	
Hämoglobin	13.6	g/dl	12.0-16.0	
Hämatokrit (Volumenfraktion)	0.40	l/l	0.35-0.47	
MCV (mittl. Zellvolumen)	89	fl	78-98	
MCH (mittl. Zell-Hb)	30	pg	27-33	
MCHC (mittl. Zell-Hb-Konz.)	34	g/dl	32-36	
RDW-CV	13	%	11-16	
Neutrophile Granulozyten abs.	3.0	G/l	2.0-7.5	
Lymphozyten abs.	2.5	G/l	1.0-4.0	
Monozyten abs.	0.7	G/l	< 1.2	
Eosinophile Granulozyten abs.	0.08	G/l	< 0.40	
Basophile Granulozyten abs.	0.0	G/l	< 0.2	
Neutrophile Granulozyten rel.	↓ 48	rel %	50-75	
Lymphozyten rel.	39	rel %	25-40	
Monozyten rel.	12	rel %	< 12	
Eosinophile Granulozyten rel.	1.3	rel %	< 4.0	
Basophile Granulozyten rel.	0.3	rel %	< 2.0	




KLINISCHE CHEMIE

CRP	↑ 28.8	mg/l	< 5.0	
Blutsenkung 1h	20	mm	< 30	
Blutsenkung 2h	40	mm	< 53	
Natrium	136	mmol/l	135-146	
Kalium	3.9	mmol/l	3.5-5.5	
Chlorid	98	mmol/l	95-110	

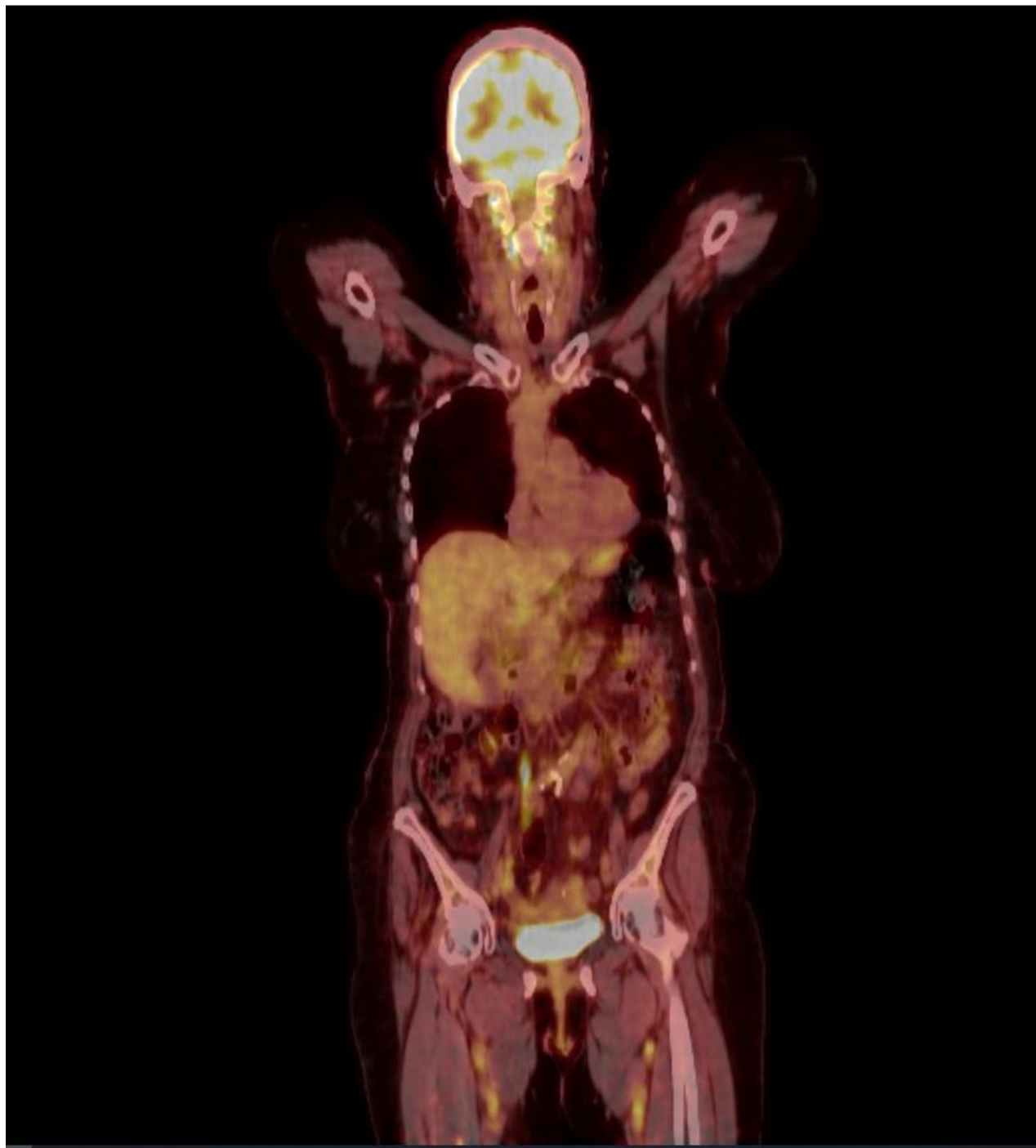
Suchergebnisse labors.at

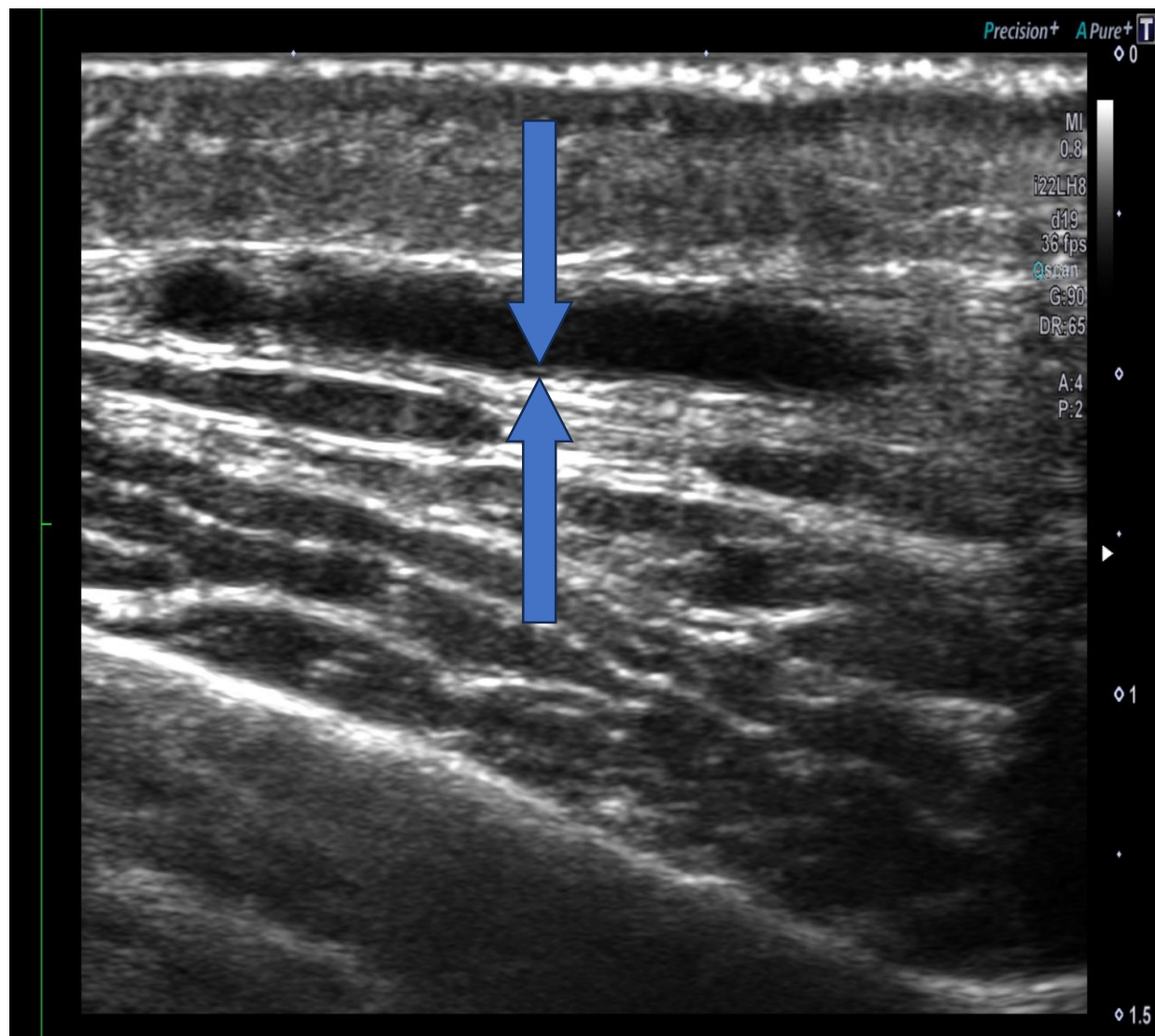
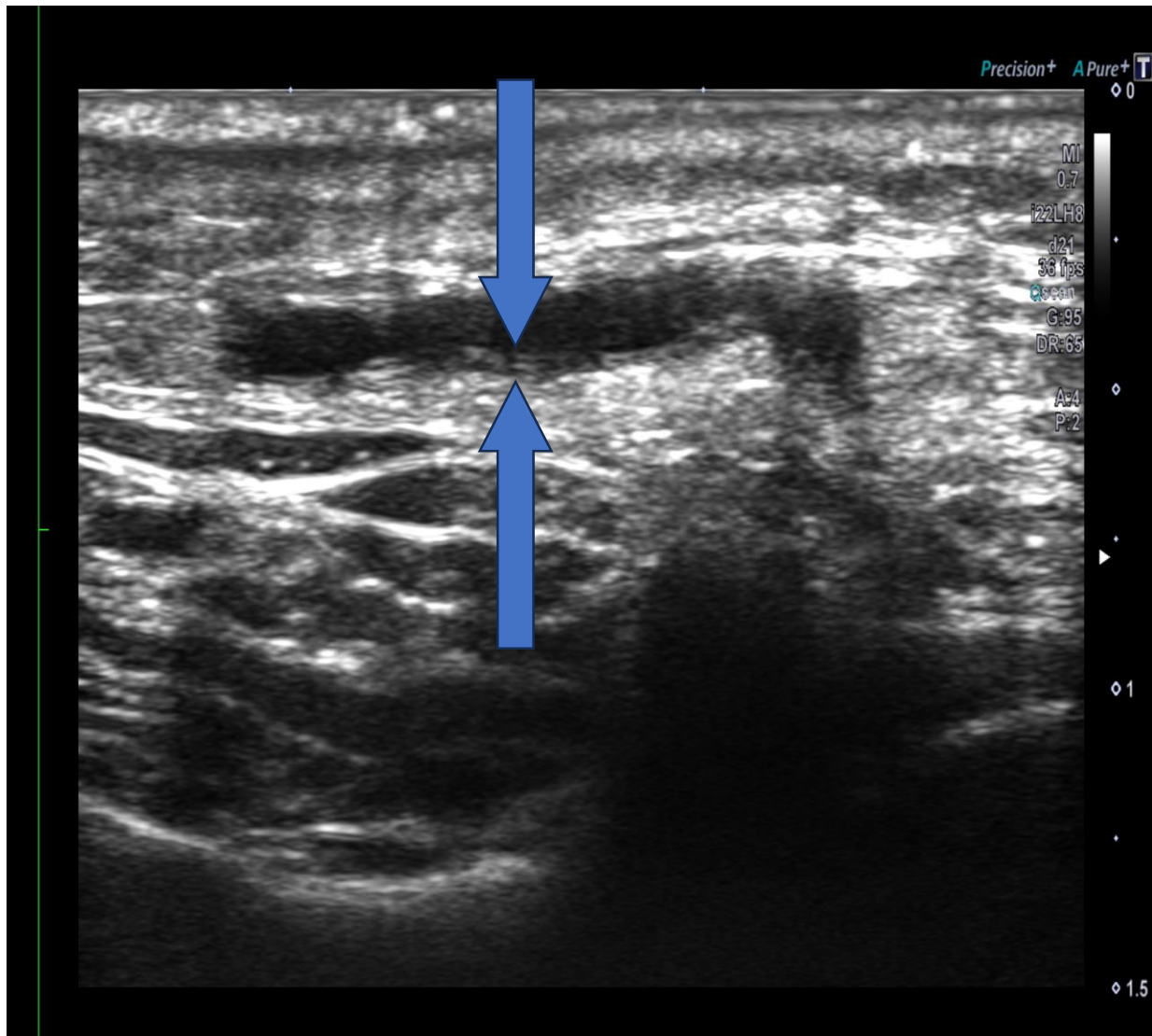
Rheumafaktor	<10	
• Rheumafaktor Isotyp IgG	6.5	
• Rheumafaktor Isotyp IgA	21.3	↑
• Rheumafaktor Isotyp IgM	5.6	
Cykl. citrul. Peptid-AK (CCP)	0.90	
• ANA-Titer (IFT)	1:1280	↑
• Nucleosomen AK	12.90	
ANA Screen (CTD)	0.10	
c-ANCA (PR-3) AK	<0.7	
p-ANCA (MPO)	<0.3	

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Verdachtsdiagnose?

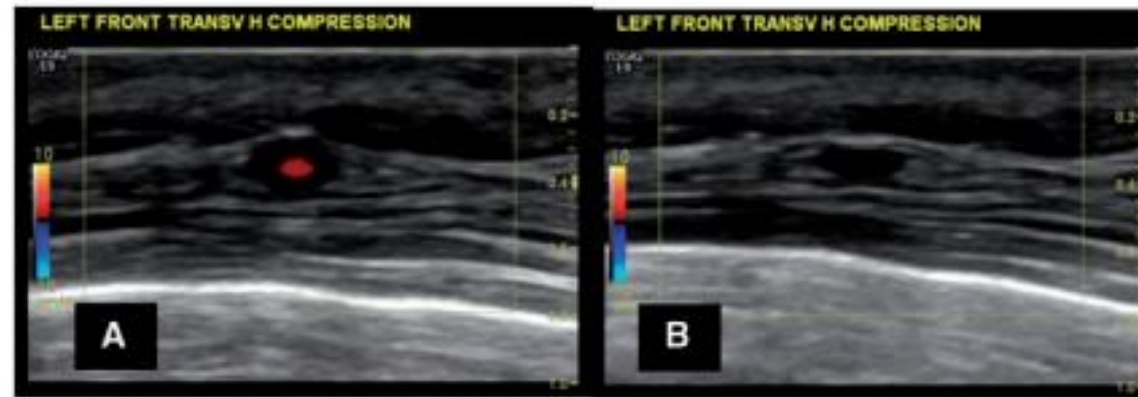




The use of ultrasound to assess giant cell arteritis: review of the current evidence and practical guide for the rheumatologist

Sara Monti^{1,2}, Alberto Floris³, Cristina Ponte^{4,5}, Wolfgang A. Schmidt⁶,

Fig. 1 US image showing a halo around the temporal artery and a positive compression sign

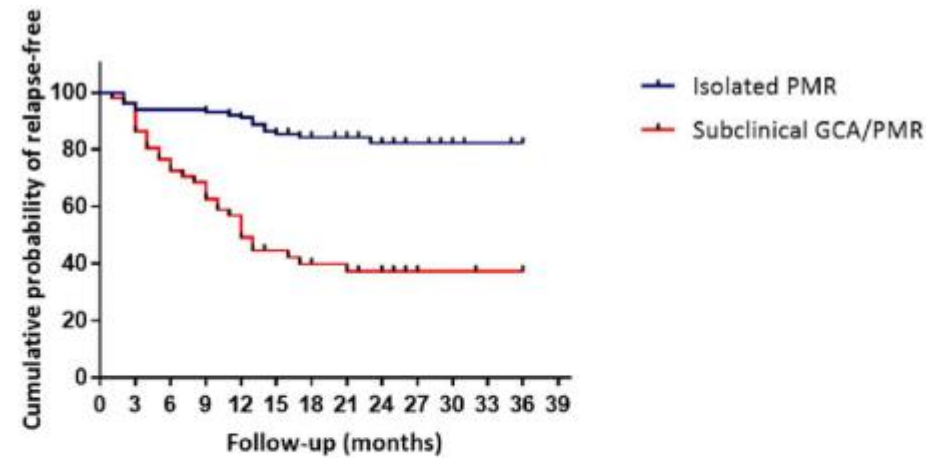


(A) Halo sign at the level of the frontal branch of the right temporal artery, transverse view, before applying compression, in a patient with active GCA. (B) Evidence of a positive compression sign with the halo persisting despite firm compression applied with the transducer.

CLINICAL SCIENCE

Subclinical giant cell arteritis increases the risk of relapse in polymyalgia rheumatica

Eugenio De Miguel ¹, Rositsa Karalilova ², Pierluigi Macchioni ³



Number at risk:

Time (months)	0	3	6	9	12	15	18	21	24	27	30	33	36	39
Isolated PMR	100	96	94	94	92	76	72	66	25	11	4	2	1	0
Subclinical GCA	50	48	38	34	28	18	15	14	10	4	3	2	2	0

Figure 2 Kaplan-Meier survival curves of relapse in patients with isolated PMR and subclinical GCA, and number at risk in the follow-up (months). GCA, giant cell arteritis; PMR, polymyalgia rheumatica.



Subclinical giant cell arteritis in new onset polymyalgia rheumatica A systematic review and meta-analysis of individual patient data

Andrea K. Hemmig^{a,1}, Daniele Gozzoli^{b,1}, Laura Werlen^c, Hannah Ewald^d, ...

Table 1
Study and patient characteristics.

Study	Location	Patients screened for GCA, n	Patients diagnosed with GCA, n (%)	Females, n (%)	Mean age (yrs ± SD)	Diagnostic procedure
Hamrin 1965 [31]	Sweden	30	11 (37)	NA	NA	TAB
Bengtsson 1981 [32]	Sweden	67	21 (31)	50 (75)	NA	TAB
Myklebust 1996 [33]	Norway	68	3 (4)	NA	NA	TAB
Kraft 1996 [34]	Germany	8	0 (0)	7 (88)	70	Ultrasound
Schmidt 2002 [35]	Germany	102	8 (8)	71 (70)	69	Ultrasound
Burg 2020 [36]	Germany	25	10 (40)	NA	NA	Ultrasound
Blockmans 1999 [37]	Belgium	5	4 (80)	5 (100)	63 ± 6	PET (4P-VS)
Moosig 2004 [38]	Germany	13	12 (92)	11 (85)	65.5	PET (Vasc-ROI)
Blockmans 2007 [39]	Belgium	35	11 (31)	20 (57)	68.5 ± 7.2	PET (TVS)
Camellino 2012 [40]	Italy	64	25 (39)	NA	NA	PET/CT (4P-VS*)
Corica 2019 [41]	Spain	52	6 (12)	NA	NA	PET/CT (qualitative)
Owen 2020 [42]	Australia	33	0 (0)	15 (45)	68.6 ± 7.4	PET/CT (4P-VS* + semi-quantitative)
Emamifar 2020 [43]	Denmark	64	6 (9)	NA	NA	PET/CT (4P-VS*)

**25% GCA
bei PMR**



A nationwide study of ocular manifestations leading to hospital contacts among patients with giant cell arteritis

Philip Therkildsen ^{a,b,*}, Annette de Thurah ^{a,b}, Mikkel Faurschou ^c, Bo Baslund ^c,

Ocular manifestations are common among patients with giant cell arteritis (GCA). Most feared is permanent visual impairment due to central retinal artery occlusion or anterior ischemic optic neuropathy [1]. Partial and complete loss of vision has been reported to occur in 2–20% of GCA patients [2–7]. Other acute ocular manifestations include diplopia and transient loss of vision (amaurosis fugax), which may precede irreversible loss of vision. However, loss of vision is seldom reported to occur after the initiation of glucocorticoid (GC) treatment [1,

2-20%
Visusverlust



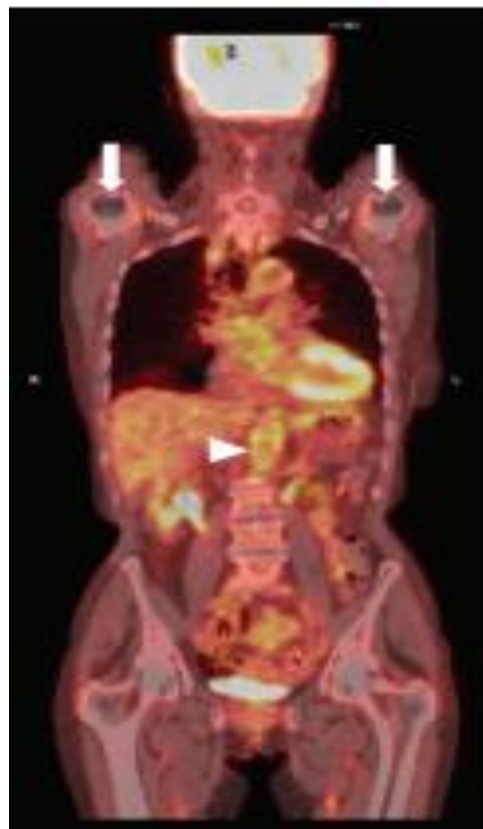
Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Prevalence and prognostic factors for aortic dilatation in giant cell arteritis – a longitudinal study

Philipp Jud^{a,*}, Nicolas Verheyen^b, Christian Dejaco^{c,d}, Elke Haas^a, Dieter Szolar^e,



Our data demonstrated that approximately one third of our GCA cohort developed AD while dilatation development affecting more frequently thoracic aorta than abdominal aorta, which is concordant to previous data [4,9].

1/3 Aortendilatation

Review Article

Giant Cell Arteritis: A Systematic Review of the Qualitative and Semiquantitative Methods to Assess Vasculitis with 18F-Fluorodeoxyglucose Positron Emission Tomography

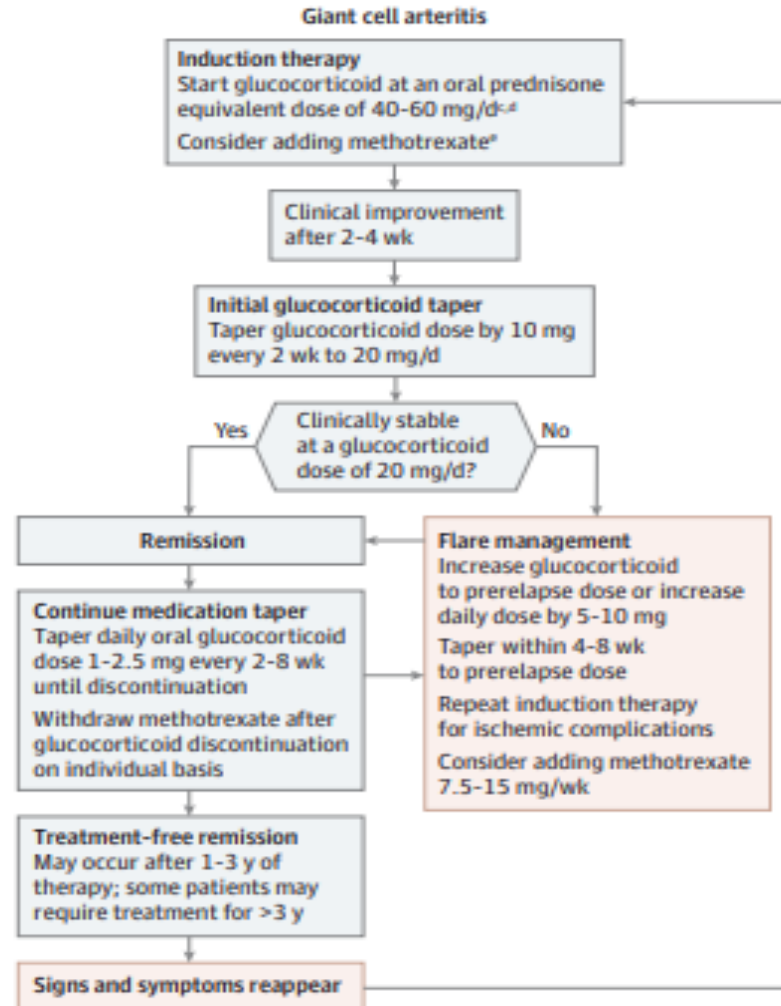
BioMed Research International
Volume 2014, Article ID 574248, 1

Therapie

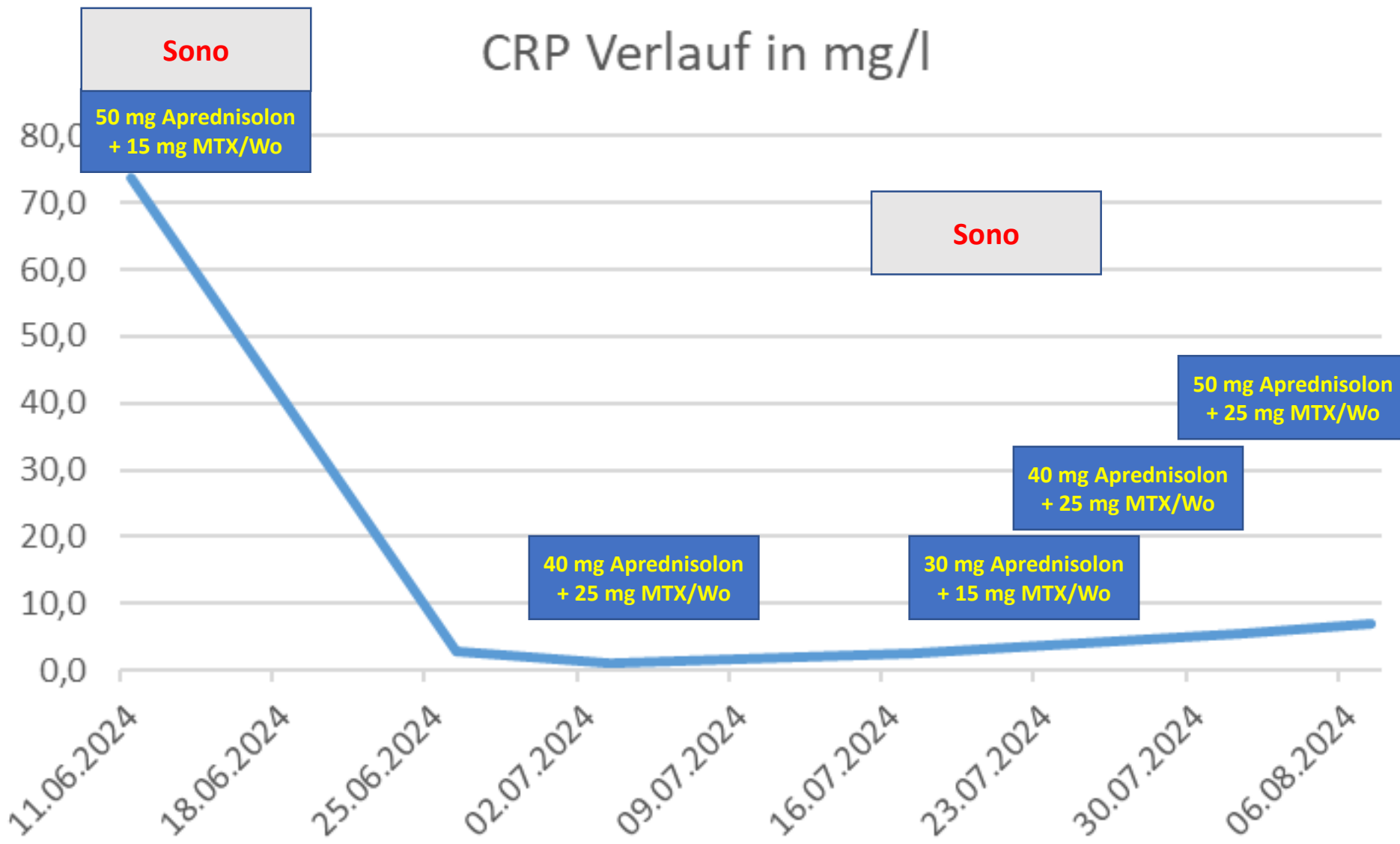
Review

Polymyalgia Rheumatica and Giant Cell Arteritis A Systematic Review

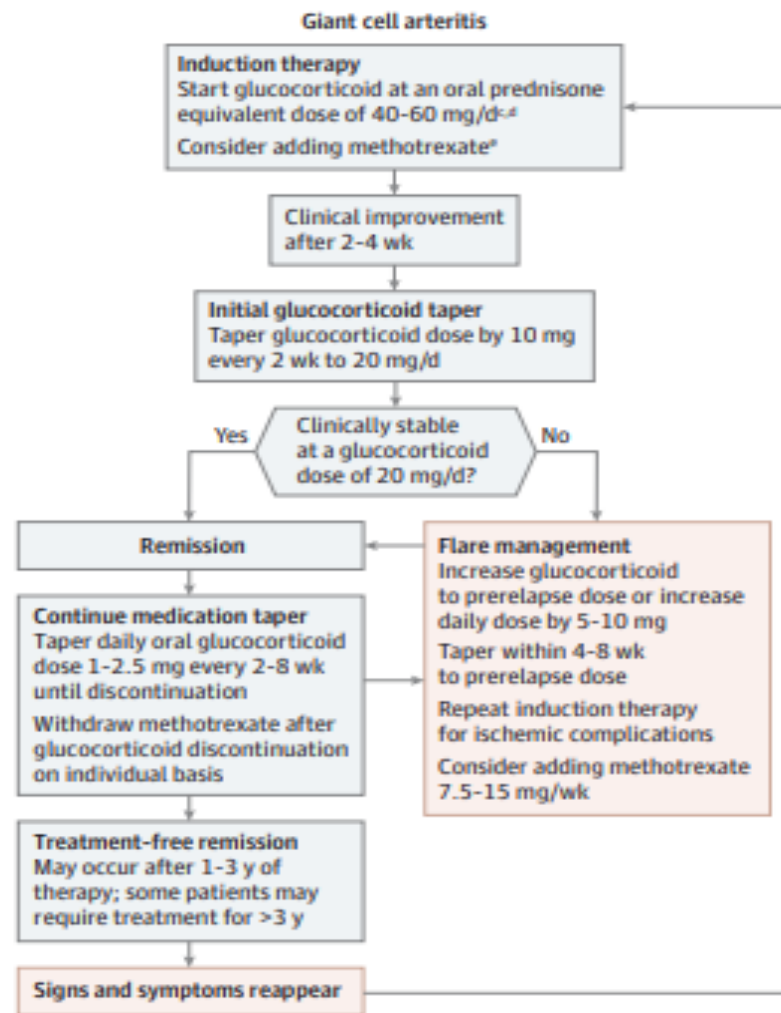
Frank Buttgereit, MD; Christian Dejaco, MD, PhD; Eric L. Matteson, MD, MPH; Bhaskar Dasgupta, MD



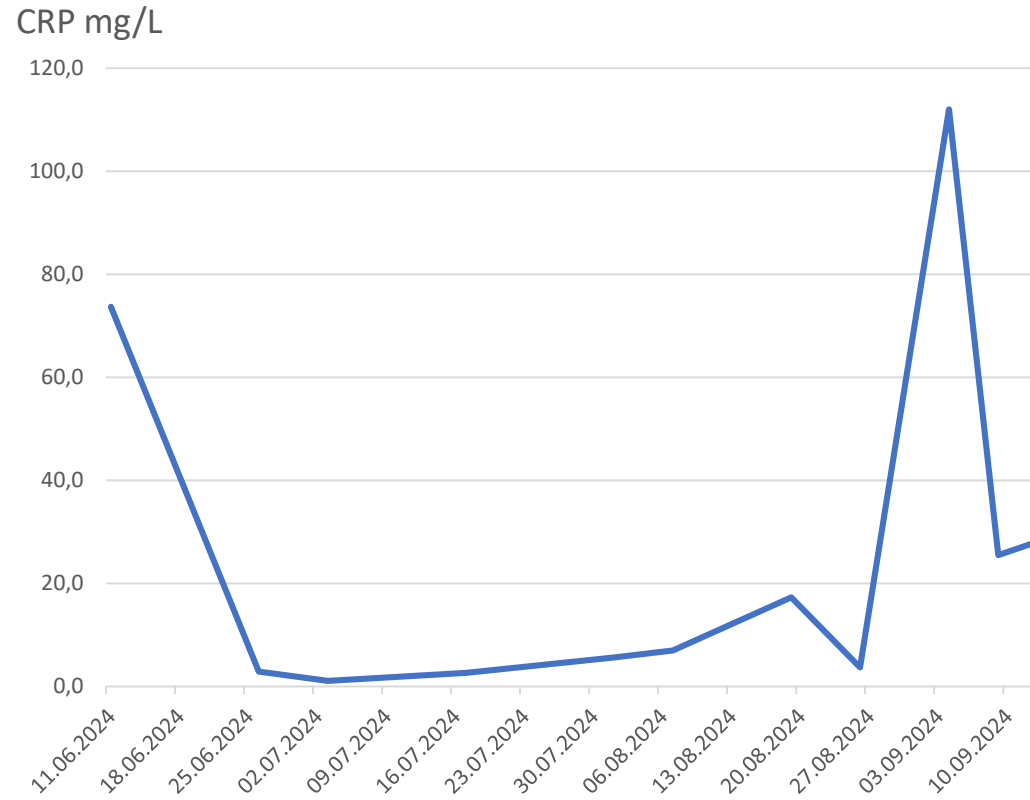
CRP Verlauf in mg/l



Vorgehen bei relapse

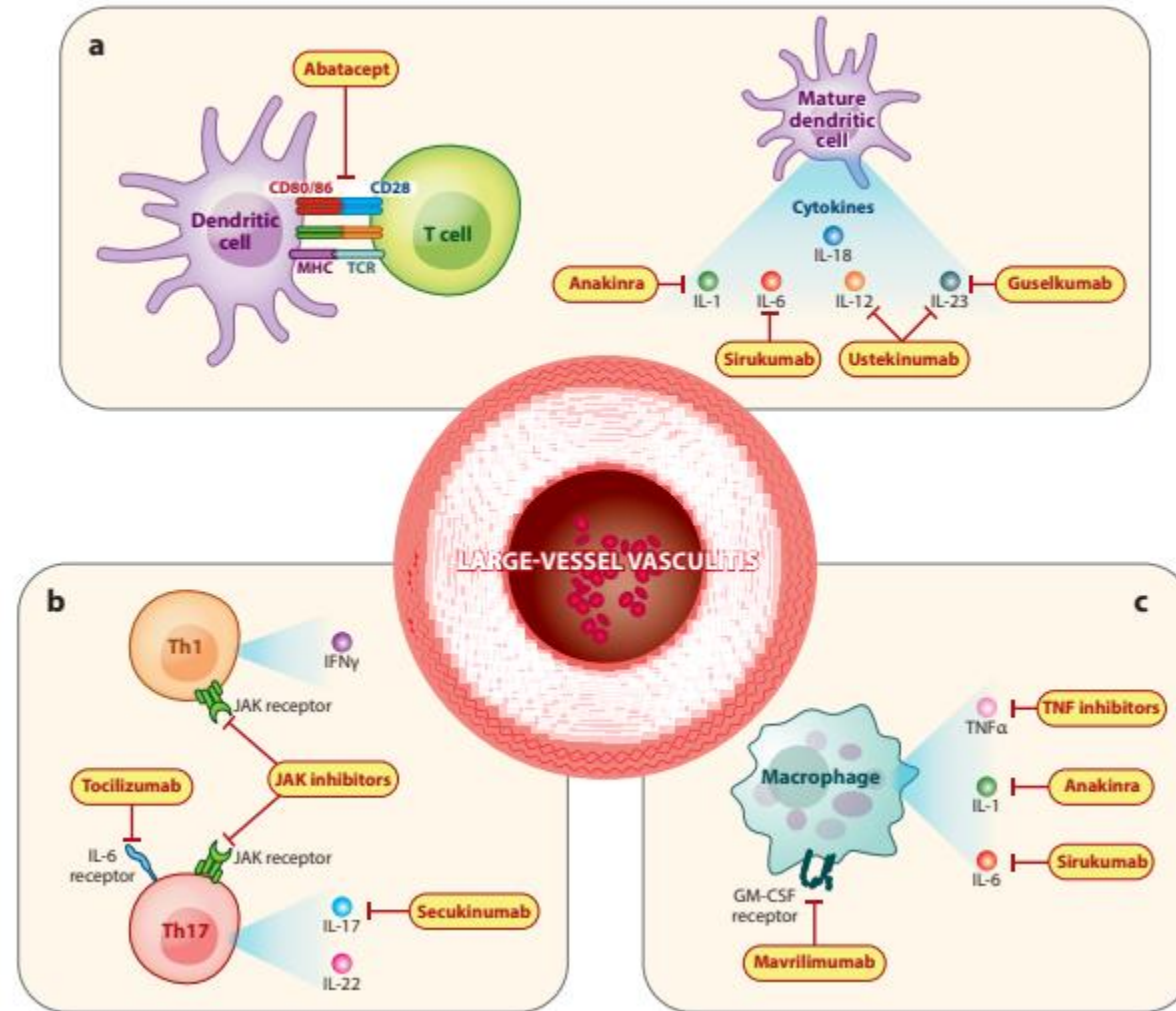


CRP-Verlauf



Verdachtsdiagnose?

New Therapeutic Approaches to Large-Vessel Vasculitis



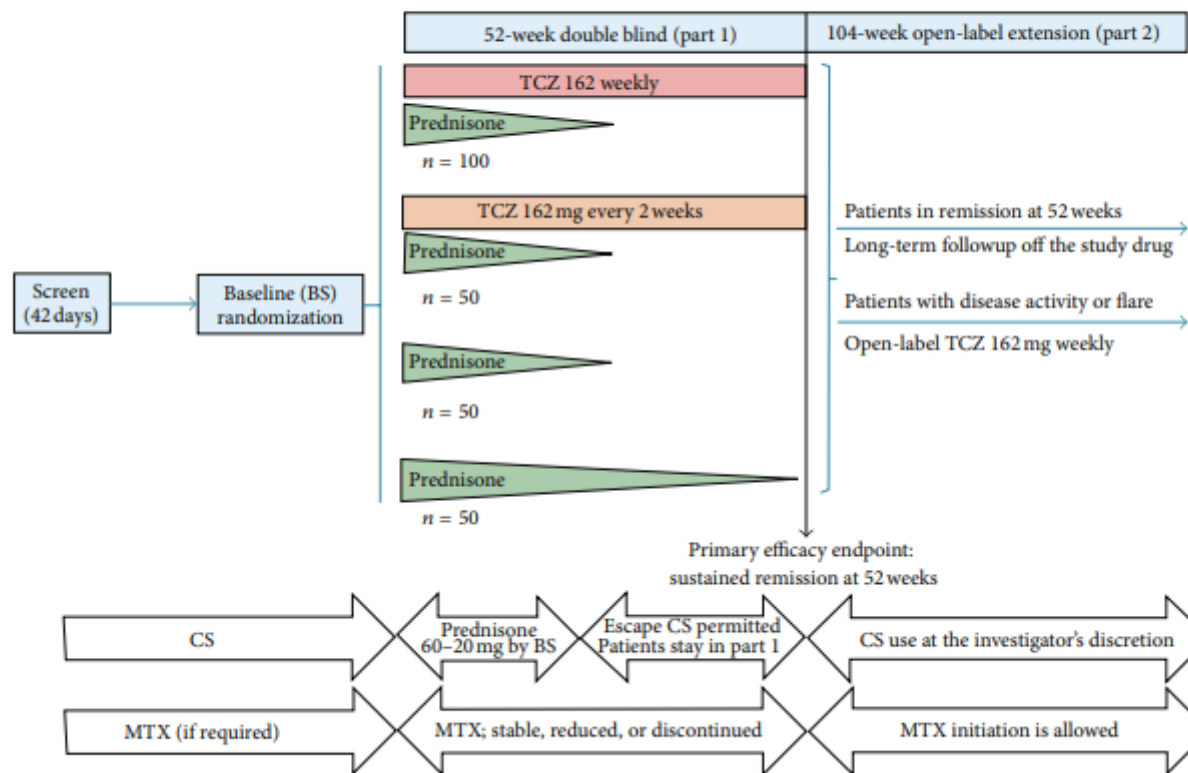


FIGURE 1: Study schema.

Cortisondosisreduktion

Weeks	Daily prednisone dose (mg) 26-week taper	Daily prednisone dose (mg) 52-week taper	Weeks	Daily prednisone dose (mg) 26-week taper	Daily prednisone dose (mg) 52-week taper
1	60	60	47	CS placebo	2
2	50	50	48	CS placebo	2
3	40	40	49	CS placebo	1
4	35	35	50	CS placebo	1
5	30	30	51	CS placebo	1
6	25	25	52	CS placebo	1
7	20	20			
After week 7, the CS dosing will be double-blinded					
8	15	17.5			
9	12.5	17.5			
10	12.5	15			
11	10	15			
12	9	12.5			
13	8	10			
14	7	10			
15	6	10			
16	6	10			
17	5	9			
18	5	9			
19	4	9			
20	4	9			
21	3	8			
22	3	8			
23	2	8			
24	2	8			
25	1	7			
26	1	7			
27	CS placebo	7			
28	CS placebo	7			
29	CS placebo	6			
30	CS placebo	6			
31	CS placebo	6			
32	CS placebo	6			
33	CS placebo	5			
34	CS placebo	5			
35	CS placebo	5			
36	CS placebo	5			
37	CS placebo	4			
38	CS placebo	4			
39	CS placebo	4			
40	CS placebo	4			
41	CS placebo	3			
42	CS placebo	3			
43	CS placebo	3			
44	CS placebo	3			
45	CS placebo	2			
46	CS placebo	2			

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 27, 2017

VOL. 377 NO. 4

Trial of Tocilizumab in Giant-Cell Arteritis

J.H. Stone, K. Tuckwell, S. Dimonaco, M. Klearman, M. Aringer, D. Blockmans, E. Brouwer, M.C. Cid, B. Dasgupta,

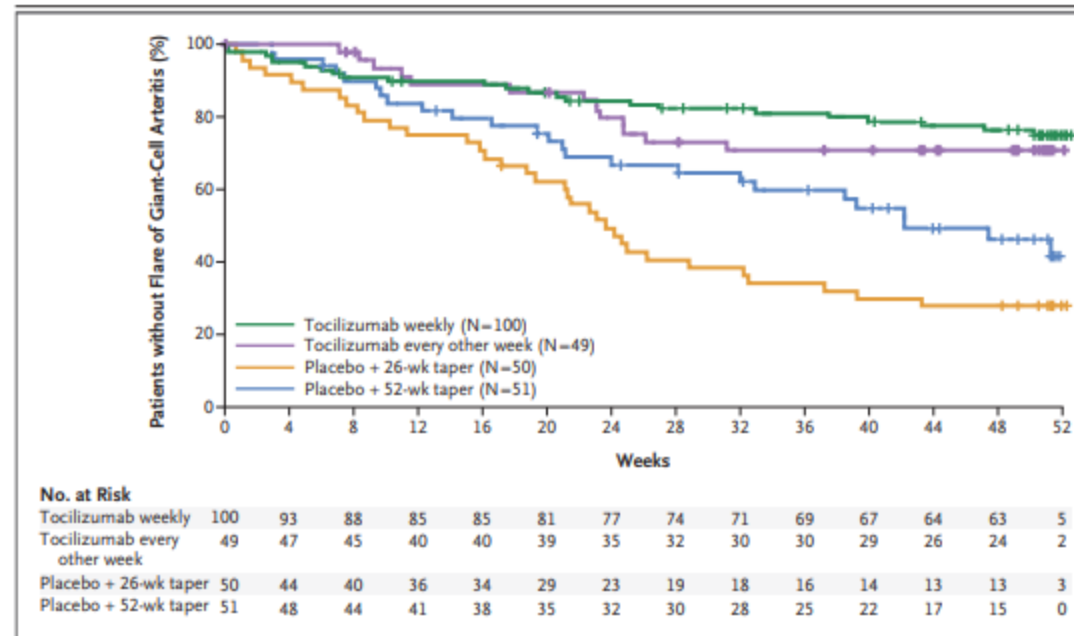
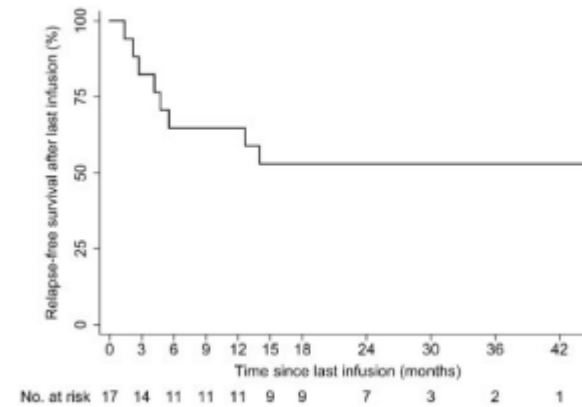
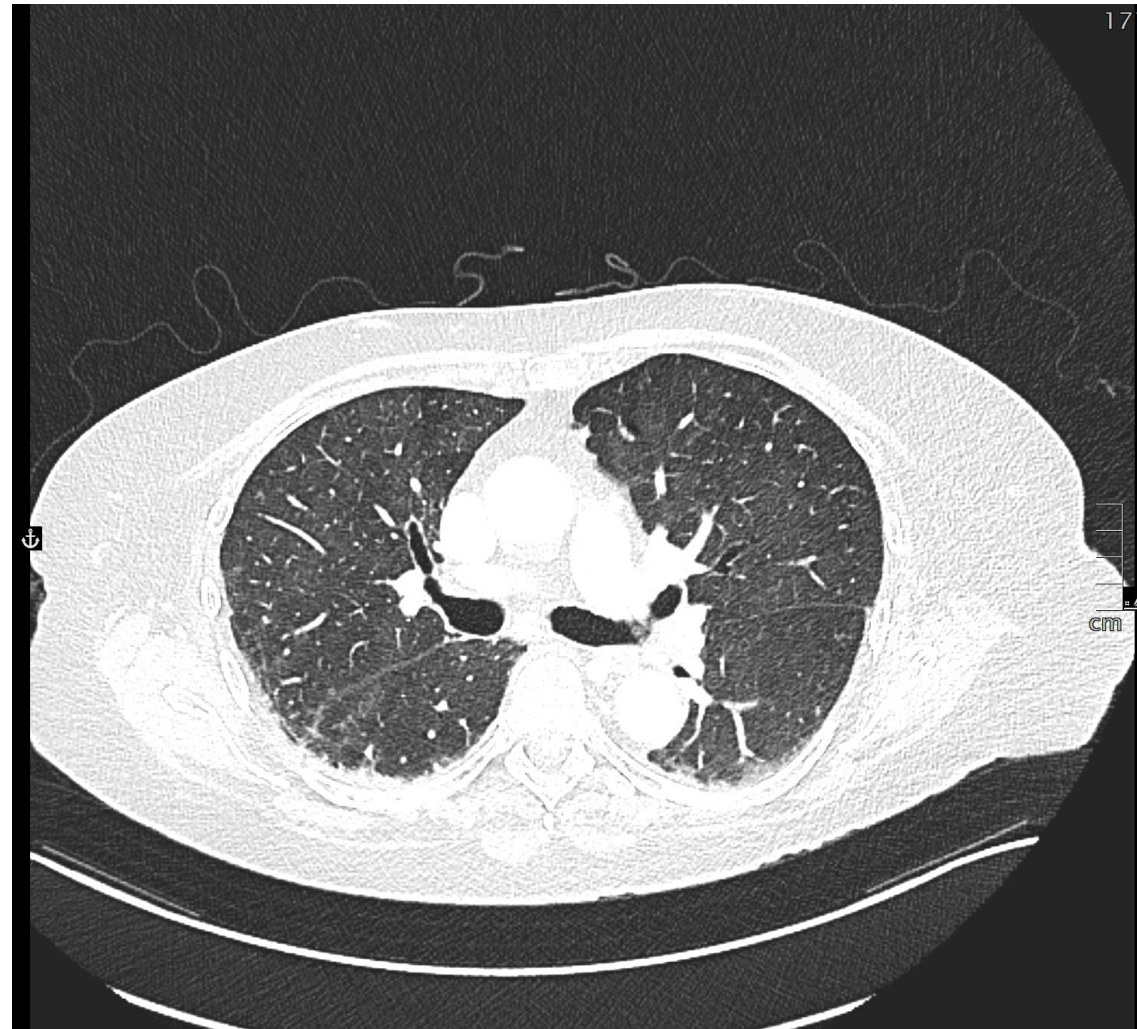


Figure 2. Time to First Flare after Clinical Remission of Giant-Cell Arteritis in All Patients.

Patients who never had remission were considered to have had a flare at week 0 (data were censored [tick marks] at that time point). Patients who withdrew from the trial before week 52 had their data censored at the time of withdrawal. The values at week 52 represent patients without flare whose week 52 visit was on day 364 of the trial only for the purpose of plotting time points; the analysis captured all the trial days associated with a week 52 visit, and appropriate censoring was applied. In a comparison with the placebo group that underwent the 26-week taper, the hazard ratio in the group that received tocilizumab weekly was 0.23 (99% CI, 0.11 to 0.46) and the hazard ratio in the group that received tocilizumab every other week was 0.28 (99% CI, 0.12 to 0.66; $P < 0.001$ for both comparisons). Absolute values for the two tocilizumab groups could not be evaluated because the median was not reached.

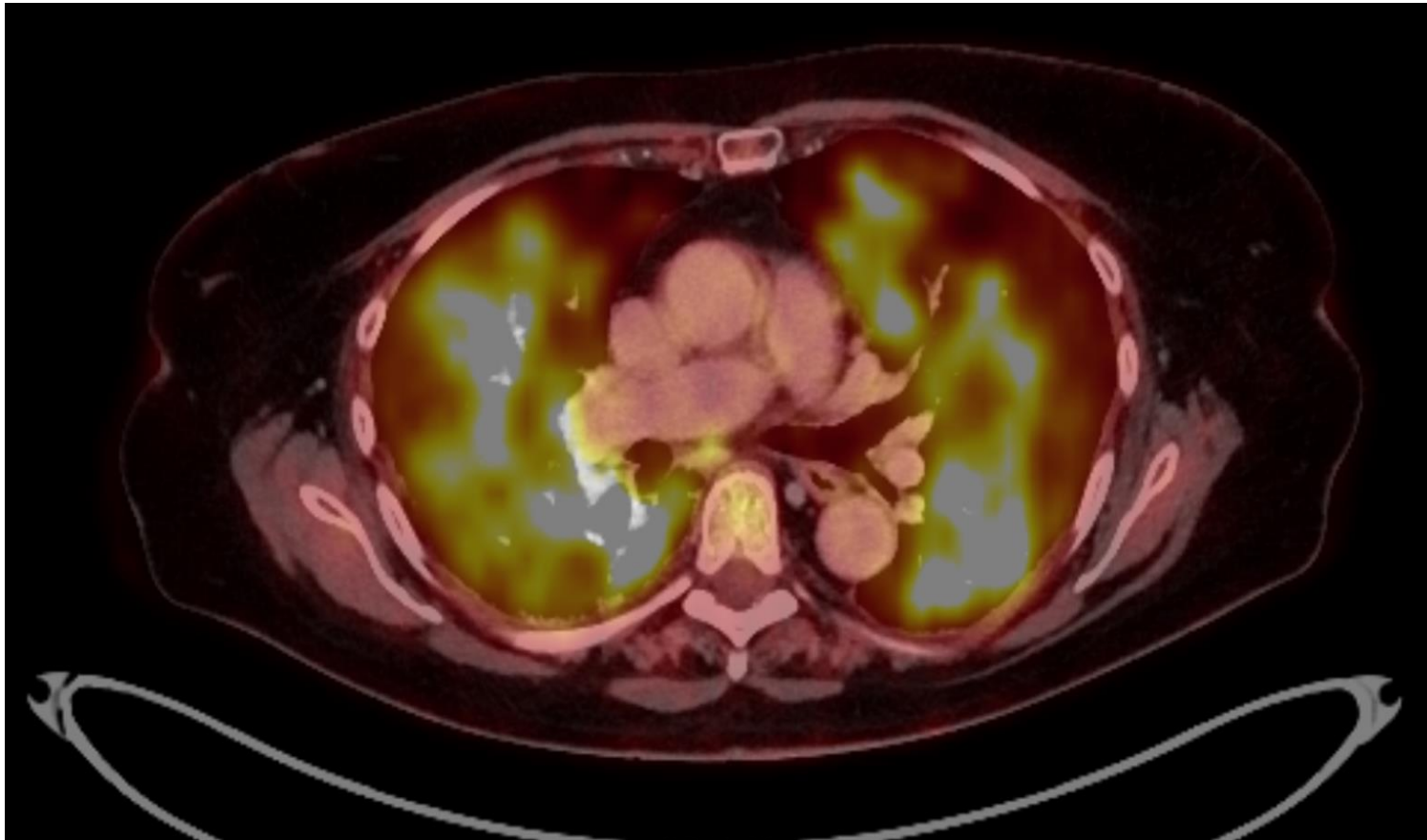
Concise report

Risk of relapse after discontinuation of tocilizumab therapy in giant cell arteritis**Sabine Adler^{1,2}, Stephan Reichenbach ², Andrea Gloor², Daniel Yerly³, Jennifer L. Cullmann⁴ and Peter M. Villiger²****FIG. 1** Kaplan–Meier curve of relapse-free survival after discontinuation of tocilizumab



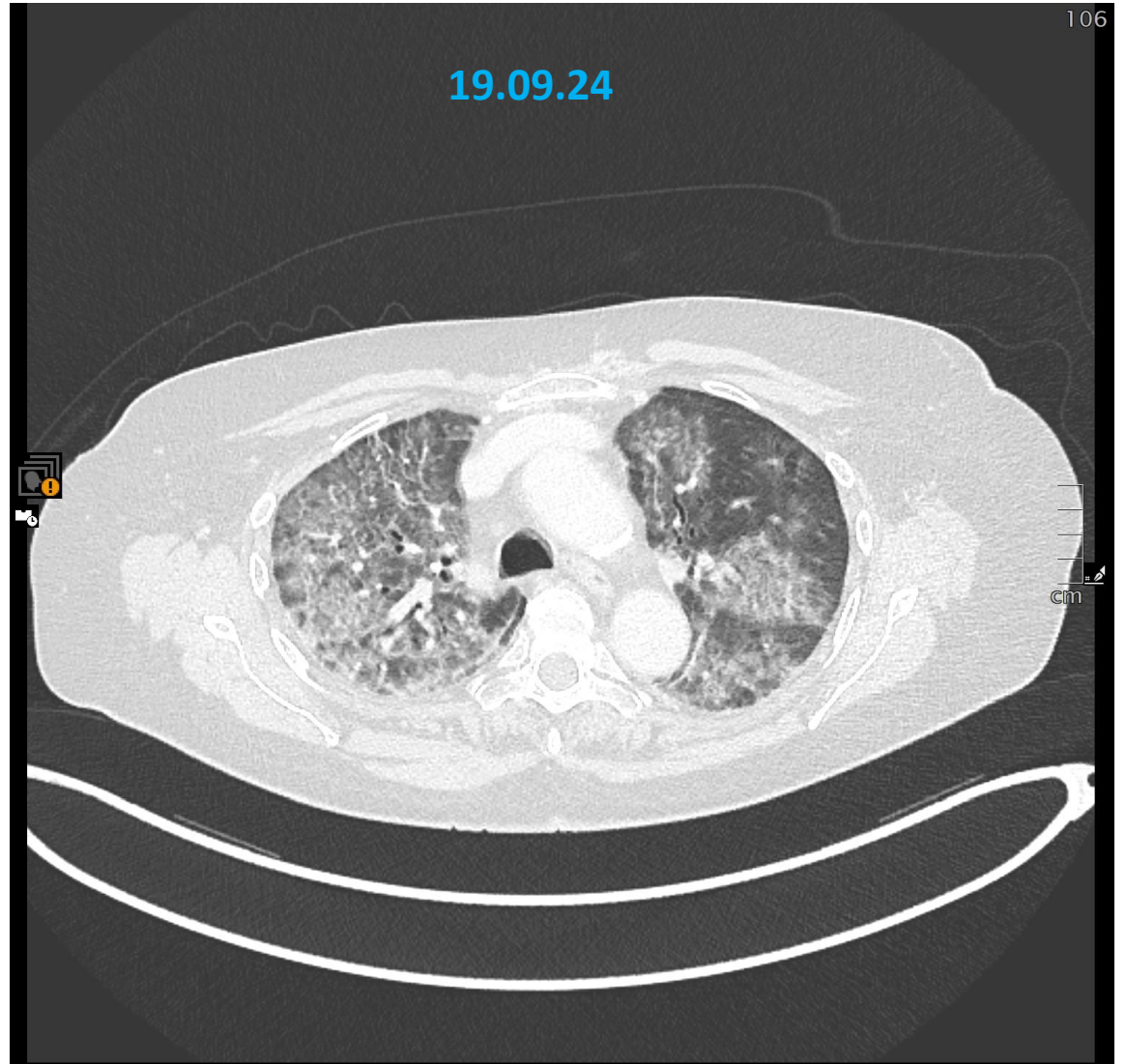
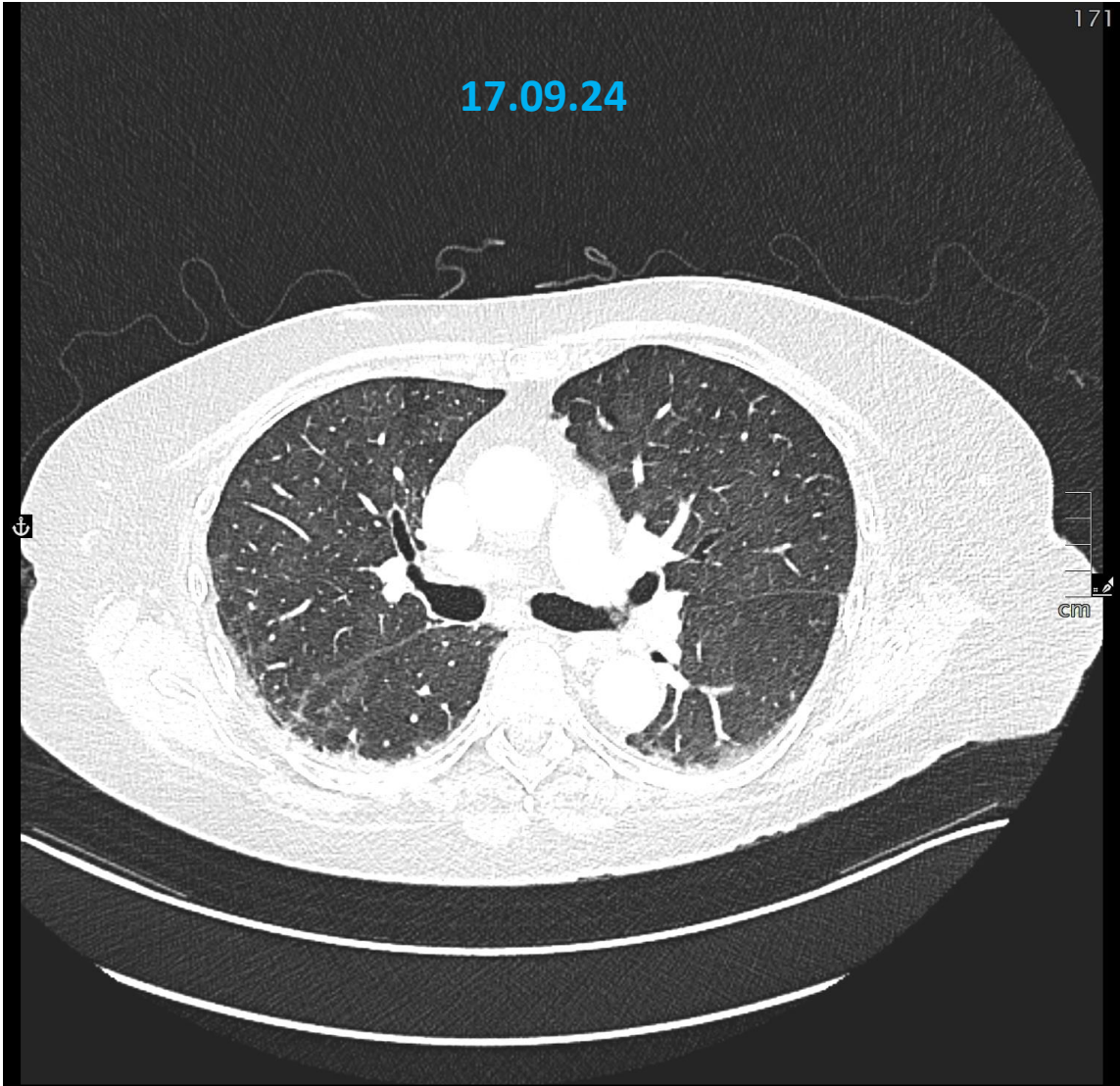
ERGEBNIS:

Beidseits Zeichen einer ILD. Intraabdominell unauffälliger Befund



ZUSAMMENFASSUNG:

- Deutliche Befundprogredienz gegenüber der rezenten Voruntersuchung vom 17.09.2024. Ausgedehnte FDG avide pulmonale Veränderungen bilateral wie oben beschrieben DD MTX induzierte Pneumonitis?
- Derzeit kein Hinweis auf floride Vaskulitis.



Verdachtsdiagnose?

Prophylactic effect of trimethoprim-sulfamethoxazole for pneumocystis pneumonia in patients with rheumatic diseases exposed to prolonged high-dose glucocorticoids

Jun Won Park,¹ Jeffrey R Curtis,² Jinyoung Moon,¹ Yeong Wook Song,¹ Suhnggwon Kim,^{3,4} Eun Bong Lee¹

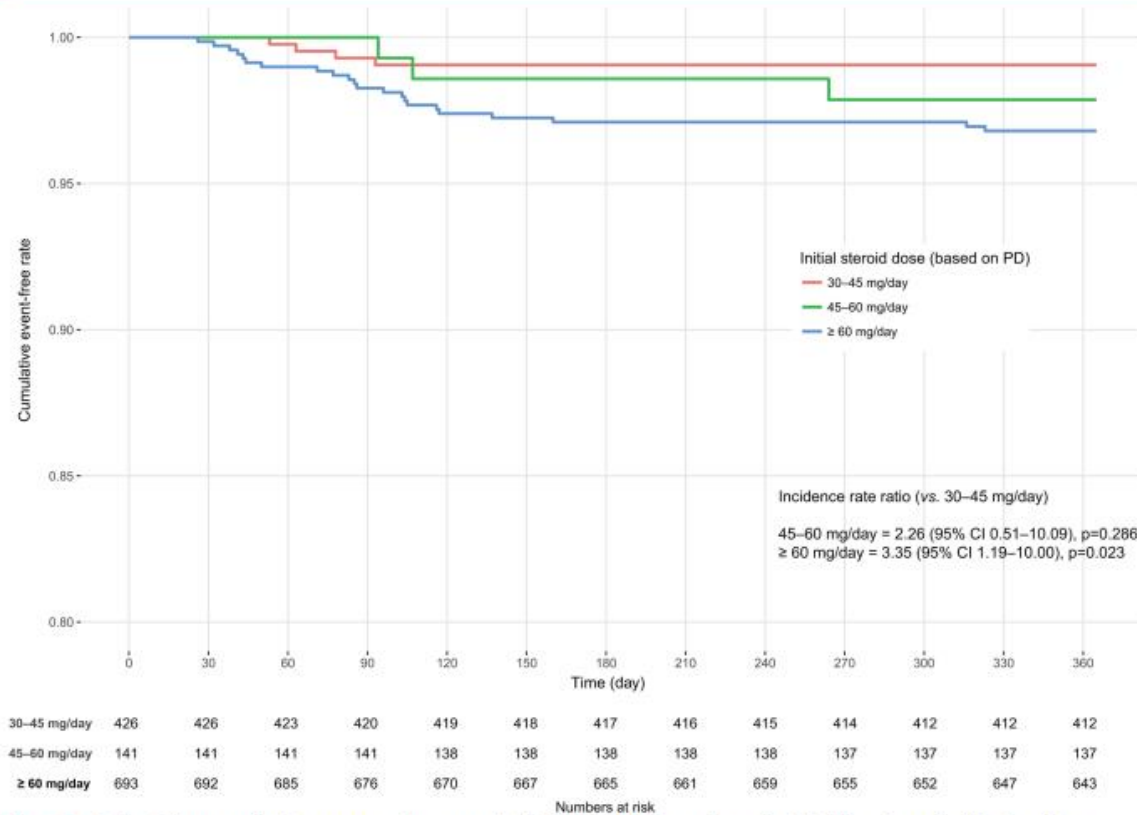


Figure 1 Kaplan-Meier curve showing pneumocystis pneumonia (PCP)-free survival according to the initial dose of steroids (30–45 mg/day prednisone, 45–60 mg/day and ≥60 mg/day) in the whole population. PD, prednisone.

Prophylactic effect of trimethoprim-sulfamethoxazole for pneumocystis pneumonia in patients with rheumatic diseases exposed to prolonged high-dose glucocorticoids

Jun Won Park,¹ Jeffrey R Curtis,² Jinyoung Moon,¹ Yeong Wook Song,¹ Suhnggwon Kim,^{3,4} Eun Bong Lee¹

Table 1 Baseline* characteristics of the whole population

	Control group (n=number of treatment episodes) (n=1260)	Prophylaxis group (n=262)
PCP-Fälle	29	1 = -93%

90% der PCP-Fälle bei Cortisondosis > 15 mg tgl. (mediane Dosis 31 mg tgl)
Mediane Zeit bis zum Auftreten der PCP 3,4 Monate (90% innerhalb der ersten 6 Monate)

TMP/SMX NW 15% (2 schwere NW Pancytopenie, Stevens-Johnson Syndrom)

2022 EULAR recommendations for screening and prophylaxis of chronic and opportunistic infections in adults with autoimmune inflammatory rheumatic diseases

George E Fragoulis ,^{1,2} Elena Nikiphorou ,^{3,4} Mrinalini Dey ,^{5,6}

Prophylaxis against *Pneumocystis jirovecii* pneumonia (PCP) should be considered in patients with AIIRD in whom high doses of glucocorticoids are used, especially in combination with immunosuppressants* and depending on the risk–benefit ratio. Prophylaxis for PCP has been mostly examined in AIIRD patients treated with glucocorticoids. Although the minimum dose and duration of glucocorticoid treatment above which prophylaxis is recommended is not defined, evidence suggests that in daily doses >15–30 mg of prednisolone or equivalent for >2–4 weeks, prophylaxis is beneficial.^{182–186} Most studies do not focus on a specific AIIRD. Therefore, it was not possible to make recommendations for PCP prophylaxis in individual diseases although the risk for PCP infection might be significantly different.¹⁸⁷ Data specifically addressing the contribution of other antirheumatic drugs in PCP development are limited.^{188–189} On the other hand, it has been shown that coadministration of immunosuppressants with glucocorticoids^{184–185–190} increase the risk for PCP.

Cotrimoxazol zur Prophylaxe und Therapie von Infektionen in der Rheumatologie

PjP-Risiko in der Rheumatologie:

Das Risiko für opportunistische Infektionen nimmt mit Art und Intensität einer spezifischen Therapie zu und korreliert mit der Grunderkrankung, der Aktivität der Erkrankung, dem Vorliegen von Komorbiditäten und der Intensität der Immunsuppression.

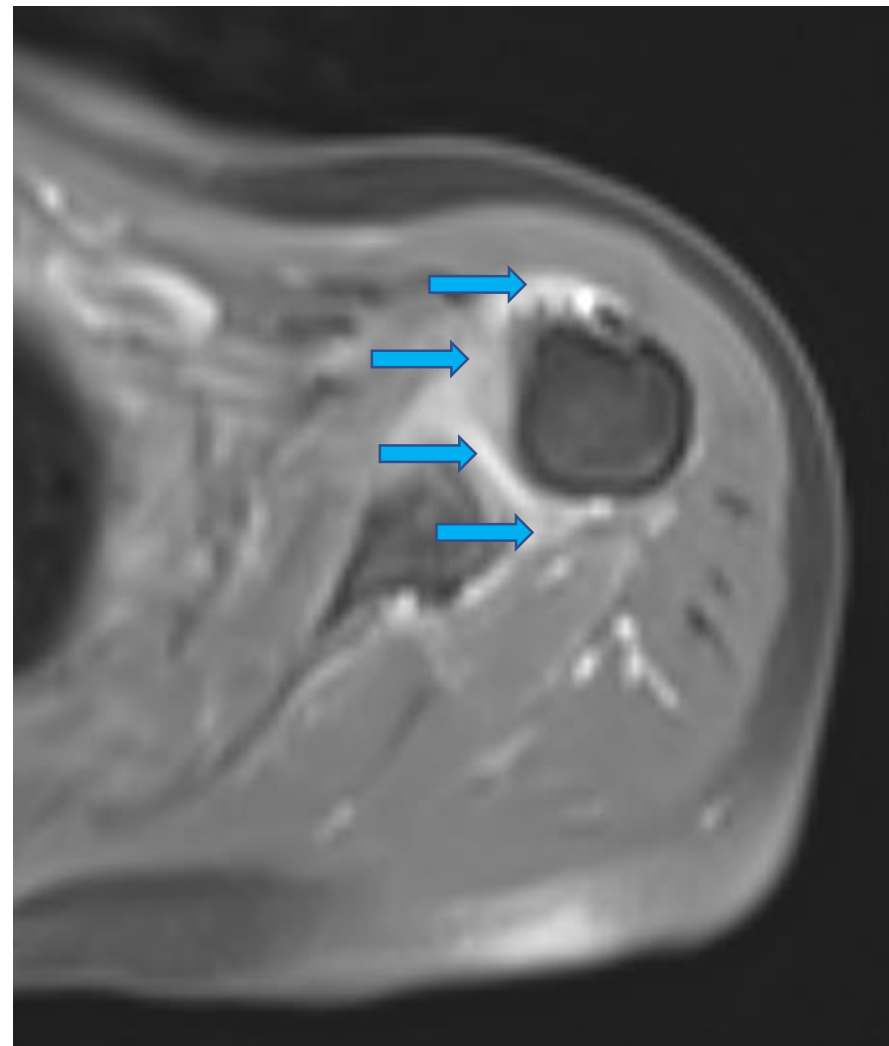
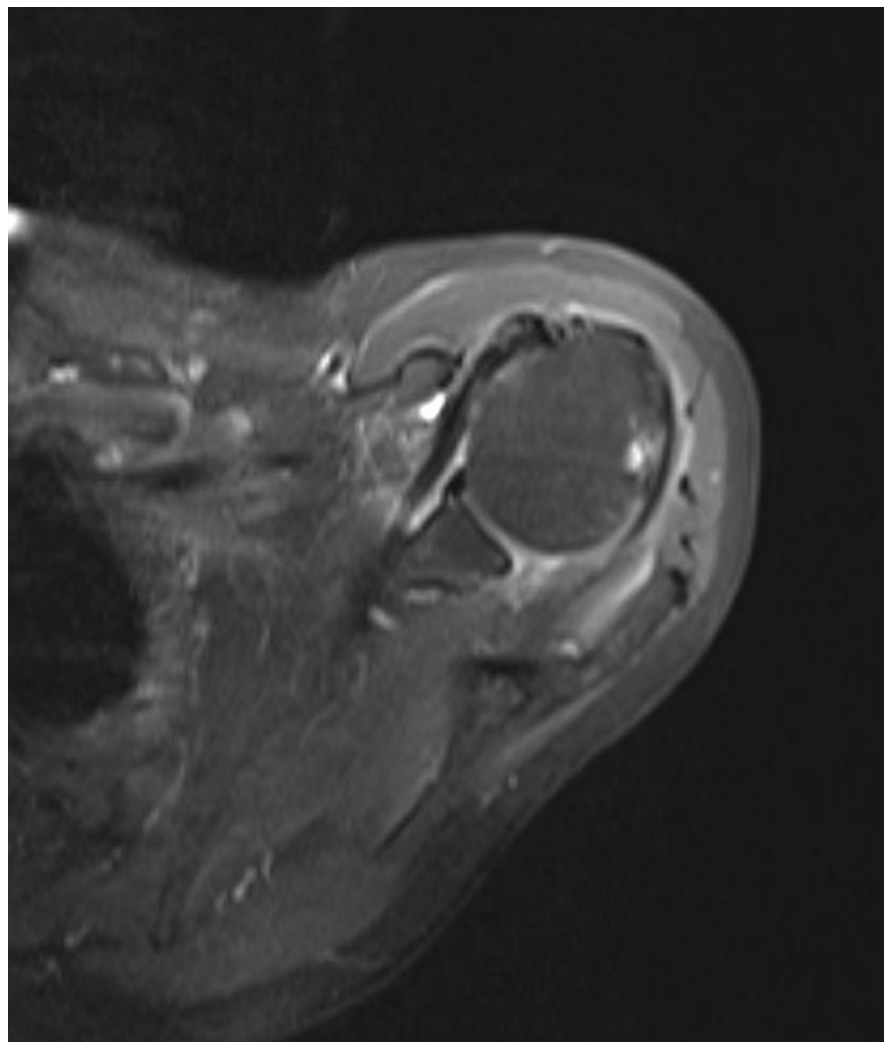
Dabei ist das Risiko für eine PjP zu einem geringeren Anteil durch die Grunderkrankung (besonders hoch bei GPA, PAN und Polymyositis (Filiatre et al.)) und zu einem höheren Anteil durch die immunsuppressive Therapie bedingt. Folgende Risikofaktoren sind bekannt:

- Glukokortikoidtherapie mit (15-)>30 mg Prednison-Äquivalent täglich für >4 Wochen (Park 2018 und 2019)
- Rituximab (Anti-CD20) Therapie (Park 2022)
- Cyclophosphamid-Therapie (Whintrop)
- CD4 (T-Helfer) Zellen <200/ μ L
- Lymphopenie
- Komorbiditäten (Alter, Gewicht, Lungenerkrankung, niedriges IgG bei RA unter b/ts DMARDs (Sonomoto))

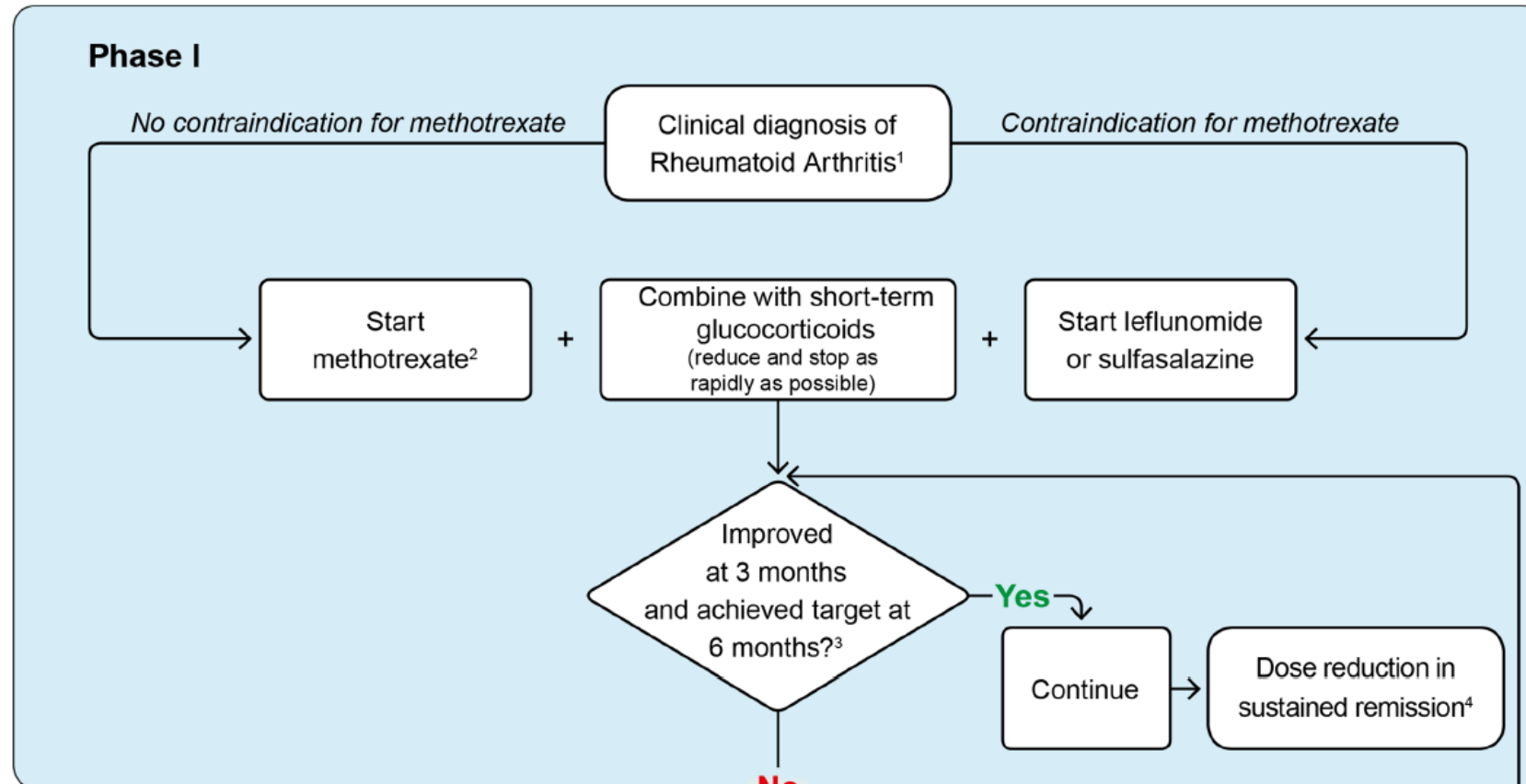
PjP-Prophylaxe:

Die Indikationsstellung für eine Cotrimoxazol-Prophylaxe beruht auf der Basis von Evidenz und Empfehlungen (u. a. Yates, Fanourakis, Fragoulis). Diese besagen, dass eine Prophylaxe gegen PjP bei Patient:innen mit entzündlich-rheumatischen Systemerkrankungen in Betracht gezogen werden sollte, bei denen hohe Dosen von Glukokortikoiden eingesetzt werden, insbesondere in Kombination mit Immunsuppressiva und in Abhängigkeit vom Nutzen-Risiko-Verhältnis (Fragoulis).

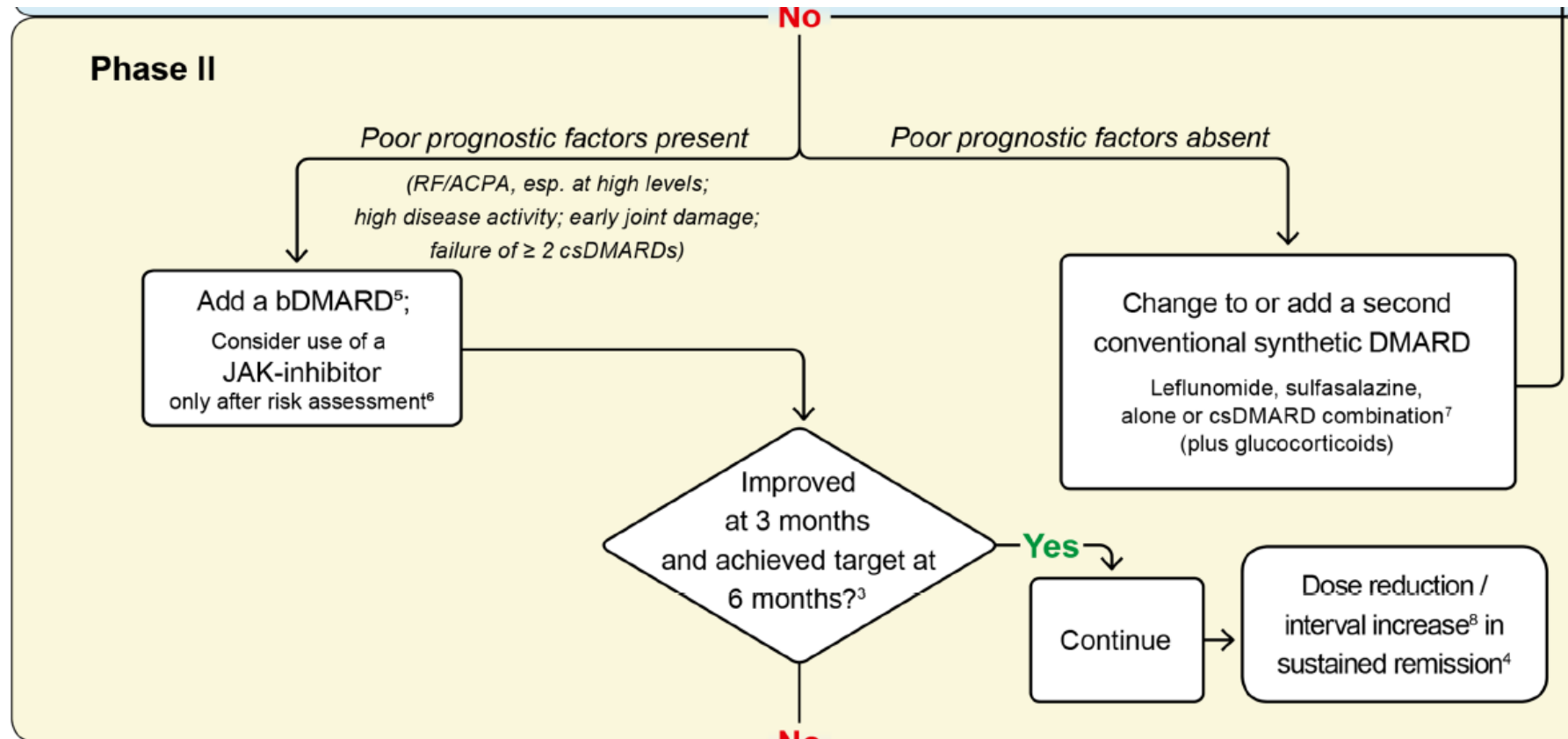
PMR DD: RA



EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update



EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update



6. The following risk factors for cardiovascular events and malignancies must be considered when intending to prescribe a JAK-inhibitor: Age over 65 years, history of current or past smoking, other cardiovascular risk factors (such as diabetes, obesity, hypertension), other risk factors for malignancy (current or previous history of malignancy other than successfully treated NMSC), risk factors for thromboembolic events (history of MI or heart failure, cancer, inherited blood clotting disorders or a history of blood clots, as well as patients taking combined hormonal contraceptives or hormone replacement therapy, undergoing major surgery or immobile)

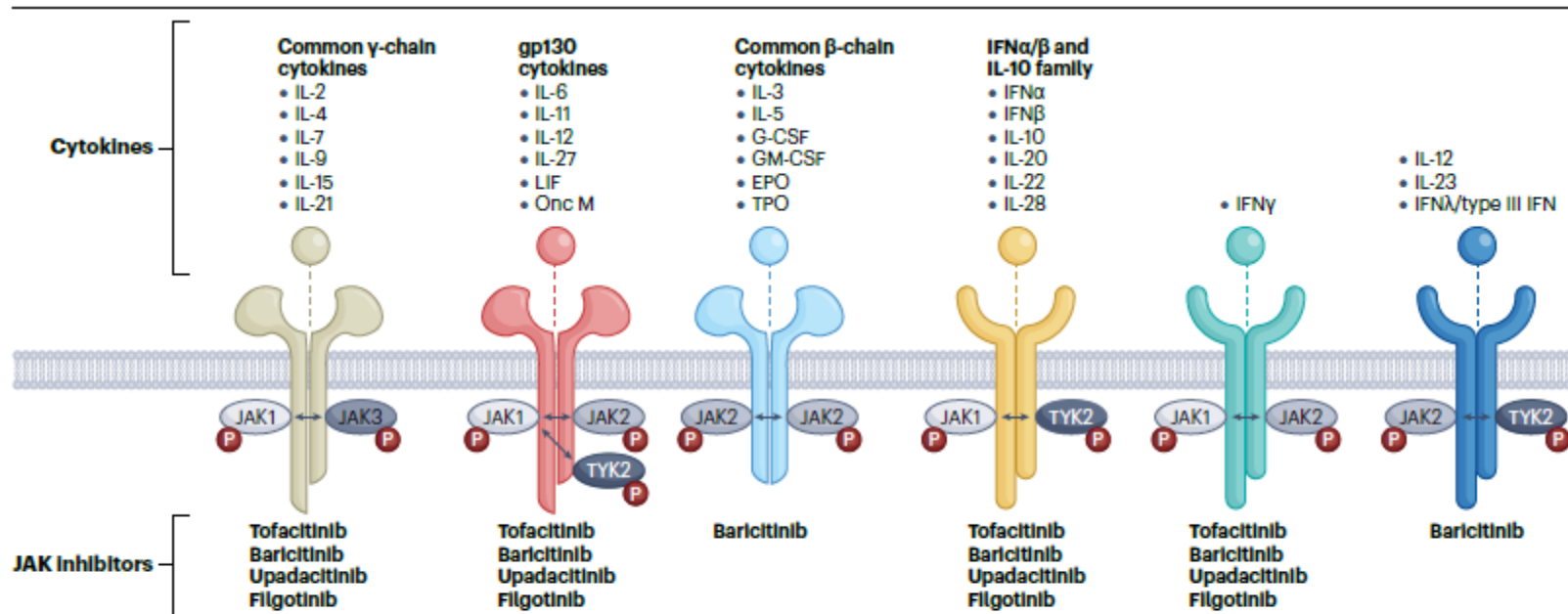
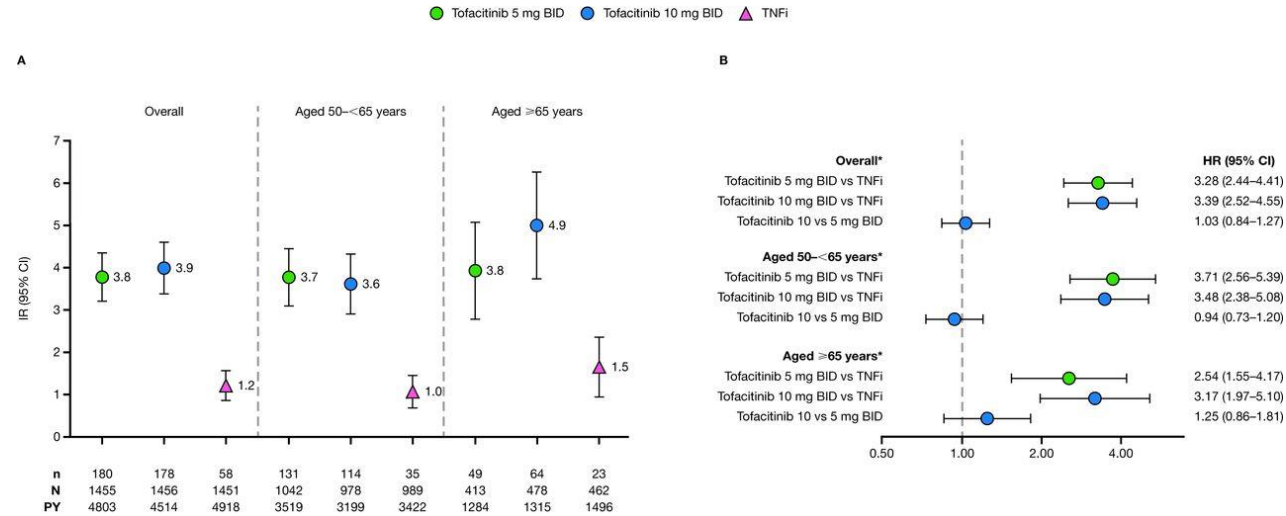


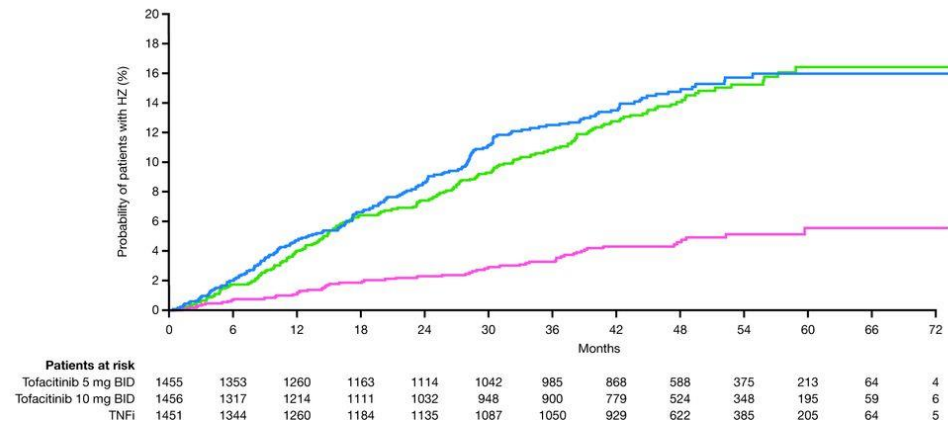
Fig. 1 | Cytokine signalling through JAKs and JAK inhibitors. The various classes of cytokines signal through different combinations of the Janus kinases (JAKs) JAK1, JAK2, JAK3 and TYK2. Among the four JAK inhibitors approved for the treatment of rheumatoid arthritis, tofacitinib and baricitinib are pan-JAK inhibitors, whereas upadacitinib and filgotinib are JAK1-selective.

EPO, erythropoietin; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; gp, glycoprotein; IFN, interferon; LIF, leukaemia inhibitory factor; Onc M, oncostatin M; TPO, thrombopoietin.

(A) IRs (patients with first events/100 PY; 95% CIs) and (B) HRs (95% CIs) for all HZ (non-serious/serious), overall and stratified by age; and (C) cumulative probabilities of experiencing a first HZ (non-serious/serious) event (Kaplan-Meier method), in ORAL Surveillance.



C

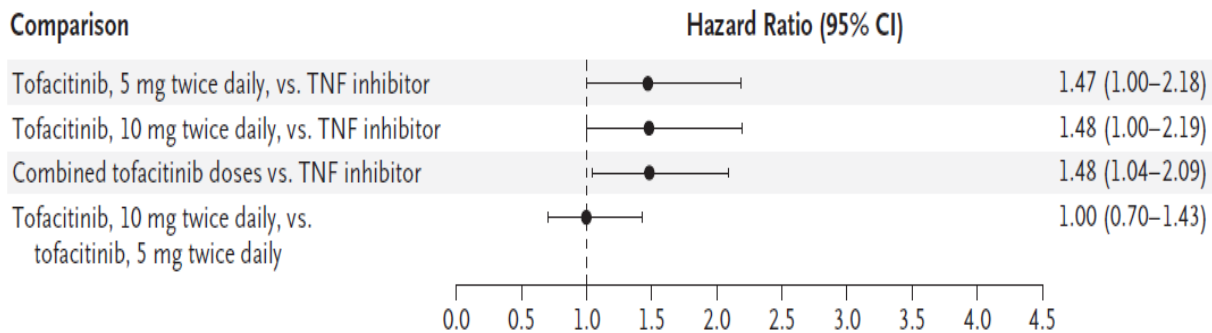


ORIGINAL ARTICLE

Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis

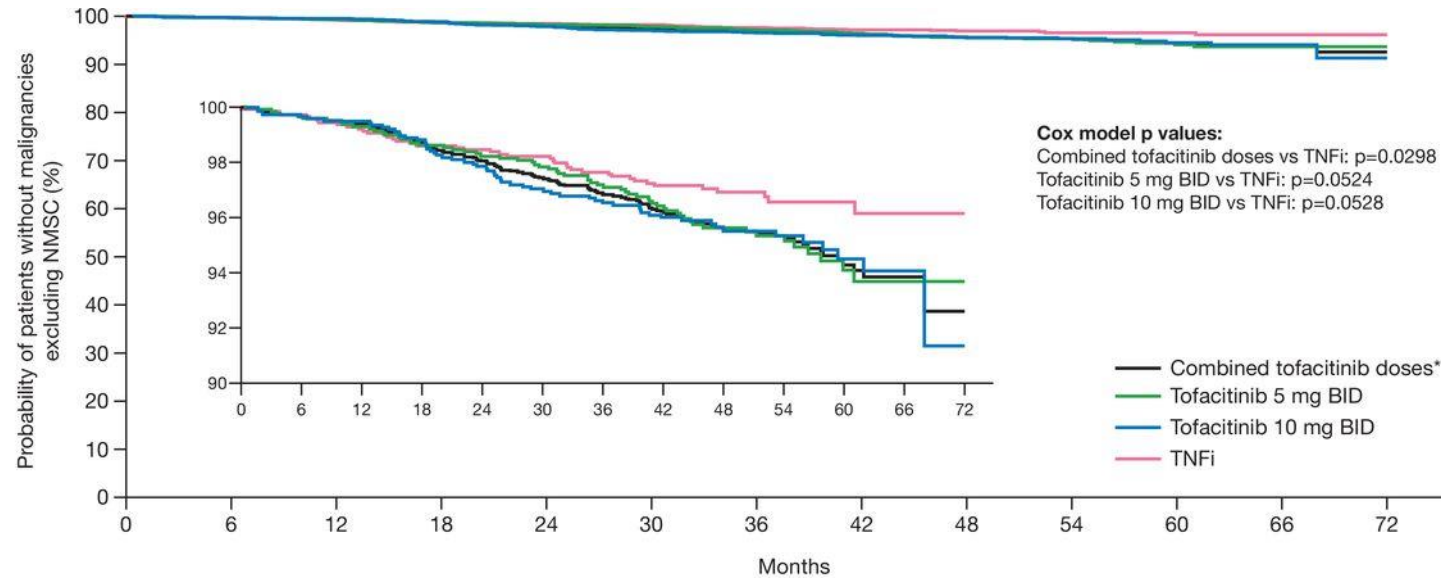
Steven R. Ytterberg, M.D., Deepak L. Bhatt, M.D., M.P.H.,

A Hazard Ratio for Cancers, Excluding NMSC



Taken together, these results show the higher risk of MACE and cancers with tofacitinib than with TNF inhibitors. The efficacies of tofacitinib and TNF inhibitors were similar across multiple outcomes.

Kaplan-Meier plot of the probability of patients without adjudicated malignancies excluding NMSC.



Patients at risk													
	0	6	12	18	24	30	36	42	48	54	60	66	72
Combined tofacitinib doses*	2911	2780	2676	2565	2471	2395	2315	2116	1483	988	544	160	13
Tofacitinib 10 mg BID	1456	1374	1319	1262	1204	1168	1137	1028	729	491	275	79	7
Tofacitinib 5 mg BID	1455	1406	1357	1303	1267	1227	1178	1088	754	497	269	81	6
TNFi	1451	1402	1351	1296	1256	1220	1197	1098	761	486	268	85	6

New restrictions on JAK inhibitors in the EU

The European Medicines Agency (EMA) has issued new recommendations to minimise the risk of serious side-effects with JAK inhibitors, often used in chronic inflammatory disorders, including ulcerative colitis. Following similar warnings from the US FDA in 2021, the EMA advises that these drugs should be used only when there are no suitable alternatives in patients aged 65 years and older, or those with risk factors for cardiovascular disease and cancer. Therapies affected by the new warnings include upadacitinib, tofacitinib, filgotinib, baricitinib, and abrocitinib. Tofacitinib was the first JAK inhibitor to receive approval.



CrossMark

For the **EMA recommendations** see <https://www.ema.europa.eu/en/news/ema-confirms-measures-minimise-risk-serious-side-effects-janus-kinase-inhibitors-chronic>

For the **FDA requirements** see <https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-related-events-cancer-blood-clots-and-death>

For the **tofacitinib approval letter** see https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2012/203214Ori

The influence of safety warnings on the prescribing of JAK inhibitors

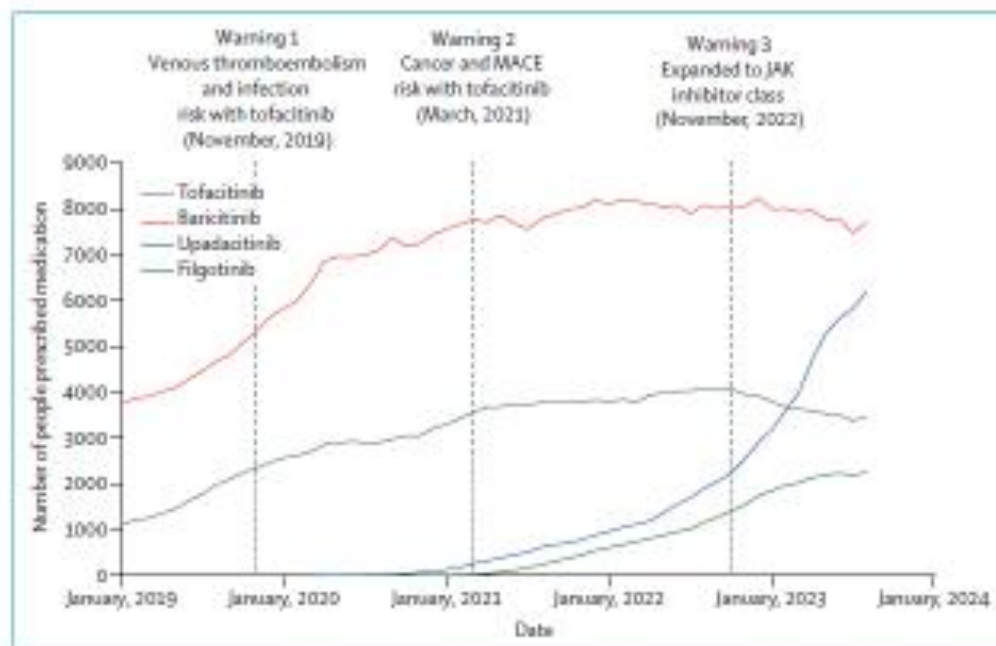


Figure: Prescribing trends for JAK inhibitors in England between Jan 1, 2019, and Aug 31, 2023

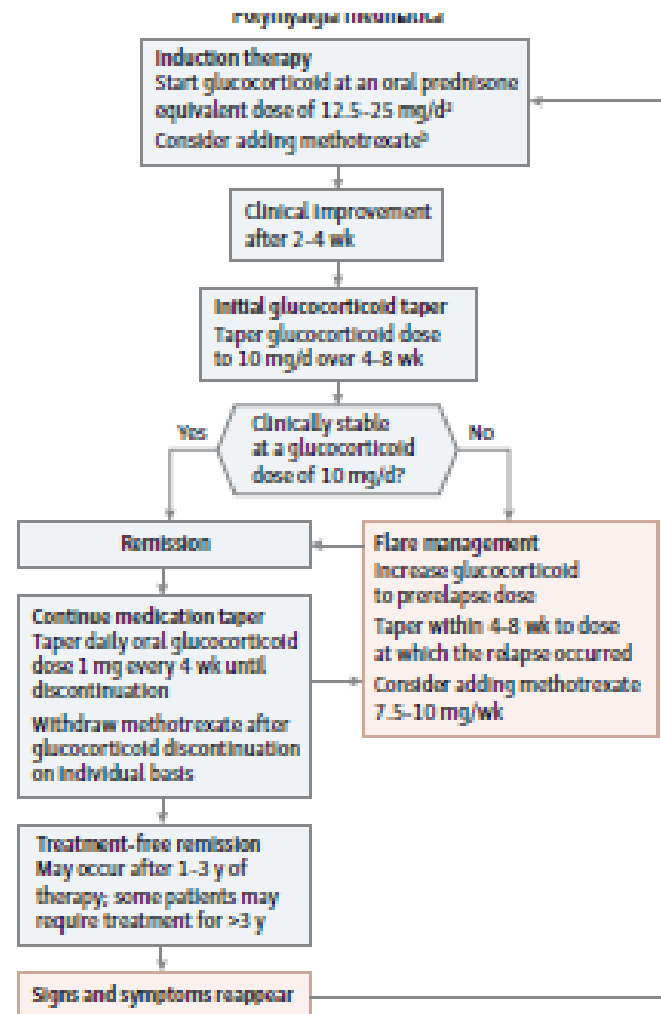
Trends in the estimated number of people prescribed tofacitinib, baricitinib, upadacitinib, or filgotinib for combined treatment indications in England between Jan 1, 2019, and Aug 31, 2023. Sequential safety warnings issued by the European Medicines Agency are denoted by vertical dashed lines. Variations in prescribing have been averaged over 3 months (see appendix p 4 for trends without smoothing). JAK=janus kinase. MACE=major adverse cardiovascular events.

Therapie

Review

Polymyalgia Rheumatica and Giant Cell Arteritis A Systematic Review

Frank Buttgereit, MD; Christian Dejaco, MD, PhD; Eric L. Matteson, MD, MPH; Bhaskar Dasgupta, MD



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

OCTOBER 5, 2023

VOL. 389 NO. 14

Sarilumab for Relapse of Polymyalgia Rheumatica during Glucocorticoid Taper

Robert F. Spiera, M.D., Sebastian Unizony, M.D., Kenneth J. Warrington, M.D., Jennifer Sloane, M.D.,

TREATMENT

Patients were randomly assigned in a 1:1 ratio to receive 52 weeks of a twice-monthly subcutaneous injection of either sarilumab (at a dose of 200 mg) plus a 14-week prednisone taper or placebo plus a 52-week prednisone taper.

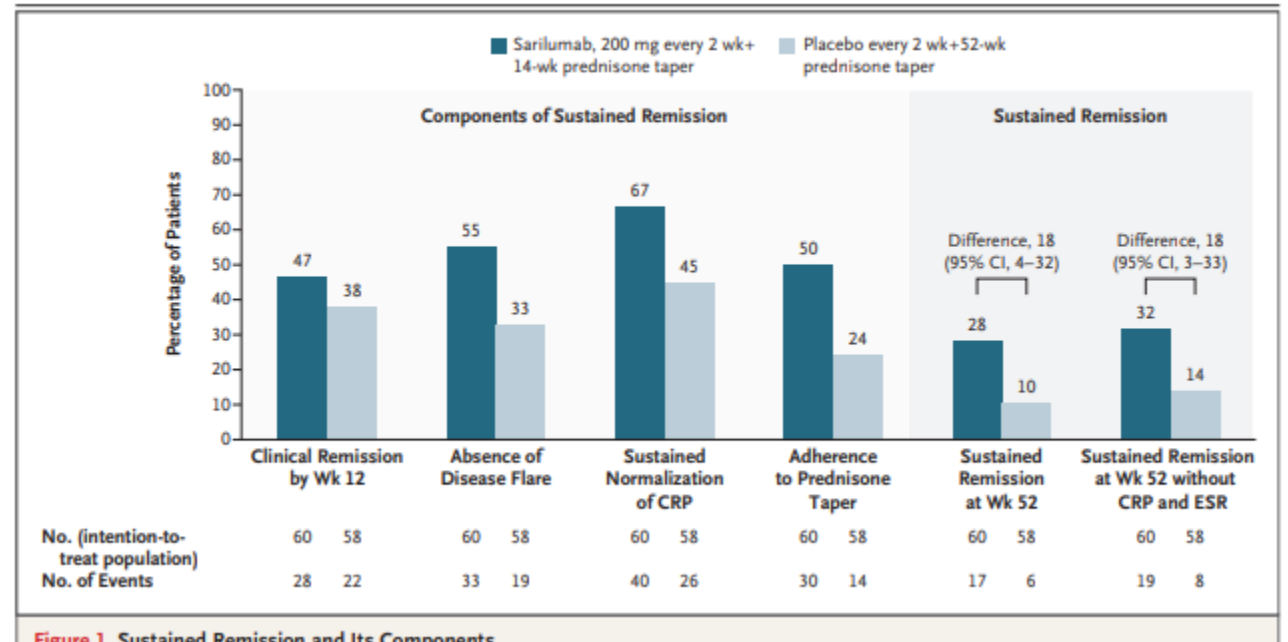


Figure 1. Sustained Remission and Its Components.



FACHINFORMATION
ZUSAMMENFASSUNG DER MERKMALE DES ARZNEIMITTELS

1. BEZEICHNUNG DES ARZNEIMITTELS

RoActemra 162 mg Injektionslösung in einer Fertigspritze

RoActemra ist indiziert für die Behandlung der Riesenzellarteriitis (RZA) bei Erwachsenen.

Original article

Risk of diverticulitis and gastrointestinal perforation in rheumatoid arthritis treated with tocilizumab compared to rituximab or abataceptClaire Rempennault ¹, Cédric Lukas¹, Bernard Combe ¹, Astrid Herrero²,

Results. With inverse probability weighting, there was an increased risk of diverticulitis in TCZ-treated patients compared with RTX- or ABA-treated patients [hazard ratio (HR)=3.1 (95% CI: 1.5, 6.3), $P = 0.002$]. Moreover, patients treated with TCZ had also an increased risk of GIP due to diverticulitis compared with those treated with RTX or ABA [HR=3.8 (1.1–13.6), $P = 0.04$], resulting in an overall increased risk of GIP [HR=2.9 (1.1–7.8),

Risiko x 3

Rheumatology key messages

- Tocilizumab is associated with an increased risk of diverticulitis.
- Tocilizumab is associated with an increased risk of gastrointestinal perforation, especially those due to diverticulitis.
- Gastrointestinal events including diverticulitis have misleading clinical presentations in RA treated with tocilizumab leading to gastrointestinal perforation.

Rheumatologie aus wissenschaftlicher Sicht – Fallbesprechung

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