CSL Vifor

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Glucokortikoid-Toxizität & Co-Morbiditäten in der Therapie der AAV

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Innsbruck

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Glukokortikoid-Toxizität & Co-Morbiditäten in der Therapie der AAV

Priv. Doz. Dr. Andreas Kronbichler PhD

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AKronbichler

Kronbichler – Conflict of interests

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Agenda

Aufbruchstimmung!

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6 Fokus auf kardiovaskuläre Komplikationen

Development of a Glucocorticoid Toxicity Index (GTI) using multicriteria decision analysis

Eli M Miloslavsky,[1] Ray P Naden,[2] Johannes W J Bijlsma,[3] Paul A Brogan,[4] E Sherwood Brown,[5] Paul Brunetta,[6] Frank Buttgereit,[7] Hyon K Choi,[8] Jean-Francois DiCaire,[9] Jeffrey M Gelfand,[10] Liam G Heaney,[11] Liz Lightstone,[12] Na Lu,[13] Dedee F Murrell,[14] Michelle Petri,[15] James T Rosenbaum,[16] Kenneth S Saag,[17] Murray B Urowitz,[18] Kevin L Winthrop,[19] John H Stone[20]

Selected items (-36 bis 439)

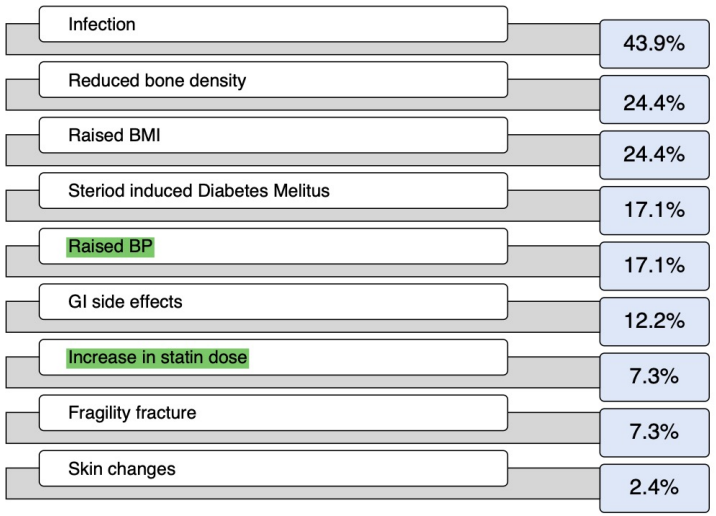
Composite GTI	Item weight	Specific List
BMI		
Improvement in BMI	–8	Major increase in BMI
No change in BMI	0	
Moderate increase in BMI	21	
Major increase in BMI	36	
Glucose tolerance		
Improvement in glucose tolerance	–8	Diabetic retinopathy
No change in glucose tolerance	0	Diabetic nephropathy
Worsening of glucose tolerance	32	Diabetic neuropathy
Worsening of glucose tolerance despite treatment	44	
Blood pressure		
Improvement in blood pressure	–10	Hypertensive emergency
No change in blood pressure	0	Posterior reversible encephalopathy syndrome
Worsening hypertension	19	
Worsening hypertension despite treatment	44	
Lipids		
Improvement in lipids	–9	
No change in lipids	0	
Worsening hyperlipidaemia	10	
Worsening hyperlipidaemia despite treatment	30	

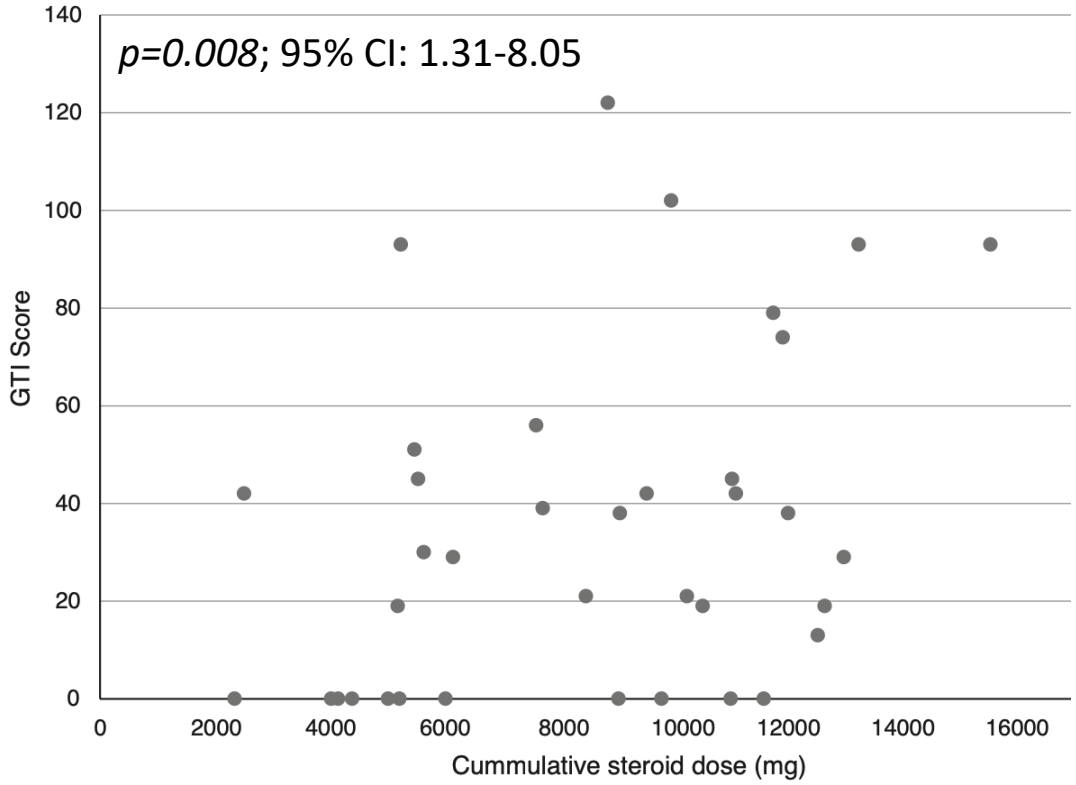
Miloslavsky EM, et al. Ann Rheum Dis 2017; **76:**543-546.

Glukokortikoid-Toxizität ”im Alltag”

19 patients with PR3-ANCA vasculitis, 24 with MPO-ANCA vasculitis

Which side effects/complications/co-morbidities are attributable to steroids alone; which contributions do other immunosuppressants or the disease have?





Floyd L, et al. Kidney360 2021; **2:**1002-1010.

Glukokortikoid-Toxizität – ADVOCATE

321 patients at week 13, 307 patients at week 26

Cumulative Worsening Score

	Avacopan group	Prednisone group	p value*
CWS			
BMI at week 13	1·1 (5·1)	3·8 (8·1)	0·0006
BMI at week 26	1·9 (6·3)	3·8 (8·2)	0·018
Glucose tolerance at week 13	0·2 (2·5)	2·9 (9·6)	0·0006
Glucose tolerance at week 26	2·9 (9·2)	3·4 (10·1)	0·64
Blood pressure at week 13	8·9 (13·2)	8·6 (12·3)	0·84
Blood pressure at week 26	13·8 (15·8)	13·8 (14·4)	0·99
Lipid metabolism at week 13	5·7 (5·7)	7·6 (6·7)	0·0052
Lipid metabolism at week 26	8·1 (6·7)	10·6 (7·5)	0·0021
Glucocorticoid myopathy at week 13	0·3 (1·6)	1·1 (6·7)	0·15
Glucocorticoid myopathy at week 26	0·4 (1·9)	1·9 (9·9)	0·059
Skin toxicity at week 13	0·8 (2·3)	1·9 (4·8)	0·0078
Skin toxicity at week 26	1·2 (3·4)	2·2 (4·7)	0·023
Neuropsychiatric effects at week 13	3·0 (12·7)	3·7 (13·2)	0·61
Neuropsychiatric effects at week 26	2·9 (11·7)	5·3 (15·7)	0·12
Infection at week 13	6·8 (22·7)	8·0 (24·6)	0·64
Infection at week 26	8·7 (25·3)	15·6 (38·6)	0·066

CWS: calculates all GC toxicity (permanent and transient – from baseline to subsequent timepoints)

Aggregate Improvement Score

	Avacopan group	Prednisone group	p value*
AIS			
BMI at week 13	0·6 (6·2)	3·7 (8·3)	0·0003
BMI at week 26	1·1 (7·7)	3·3 (8·7)	0·018
Glucose tolerance at week 13	−6·3 (13·4)	−1·3 (15·5)	0·0024
Glucose tolerance at week 26	−5·3 (16·3)	−4·5 (14·4)	0·65
Blood pressure at week 13	3·9 (19·1)	4·0 (17·9)	0·98
Blood pressure at week 26	4·5 (20·5)	4·8 (19·2)	0·90
Lipid metabolism at week 13	4·2 (7·9)	6·7 (8·2)	0·0055
Lipid metabolism at week 26	4·2 (9·4)	6·5 (9·6)	0·029
Glucocorticoid myopathy at week 13	0·2 (1·7)	0·7 (8·0)	0·44
Glucocorticoid myopathy at week 26	0·2 (1·4)	0·7 (8·6)	0·56
Skin toxicity at week 13	0·1 (3·9)	1·7 (5·0)	0·0011
Skin toxicity at week 26	−0·3 (4·3)	0·8 (4·2)	0·027
Neuropsychiatric effects at week 13	1·5 (14·6)	1·0 (17·7)	0·78
Neuropsychiatric effects at week 26	−0·9 (9·3)	−0·7 (16·7)	0·88
Infection at week 13	6·8 (22·7)	8·0 (24·6)	0·64
Infection at week 26	8·5 (25·1)	13·3 (31·3)	0·14

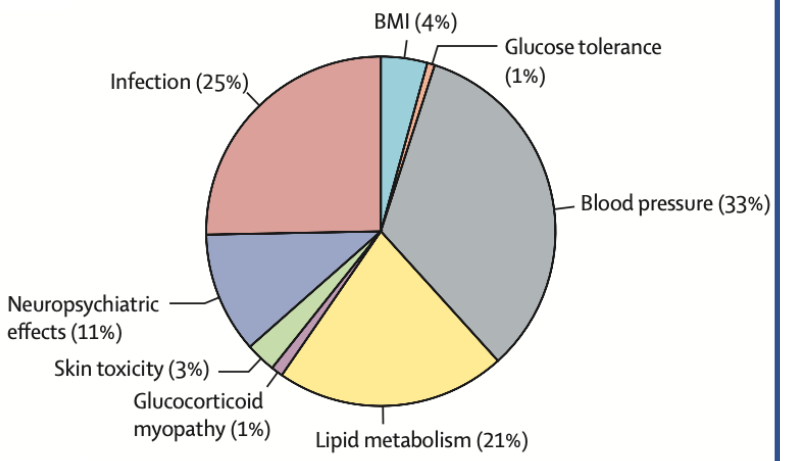
AIS: measures aggregate change (improvement and worsening) in GC toxicity (improvement in GC toxicity is assigned the same absolute weight as a worsening of GC toxicity

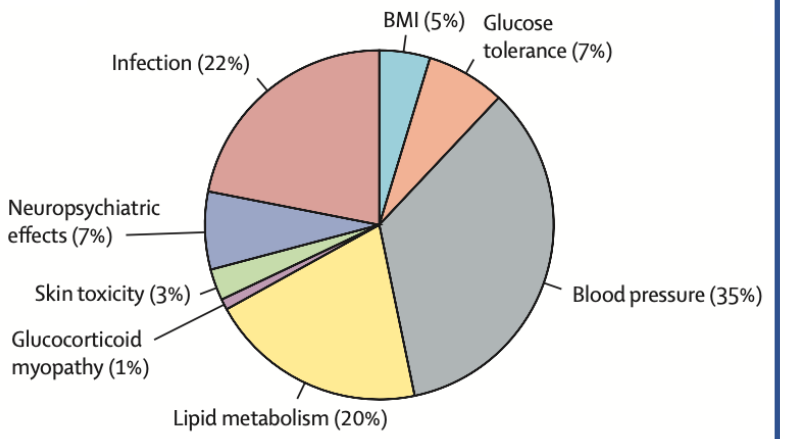
Patel NJ, et al. Lancet Rheumatol 2023; **5:**e130-38.

Glukokortikoid-Toxizität – ADVOCATE

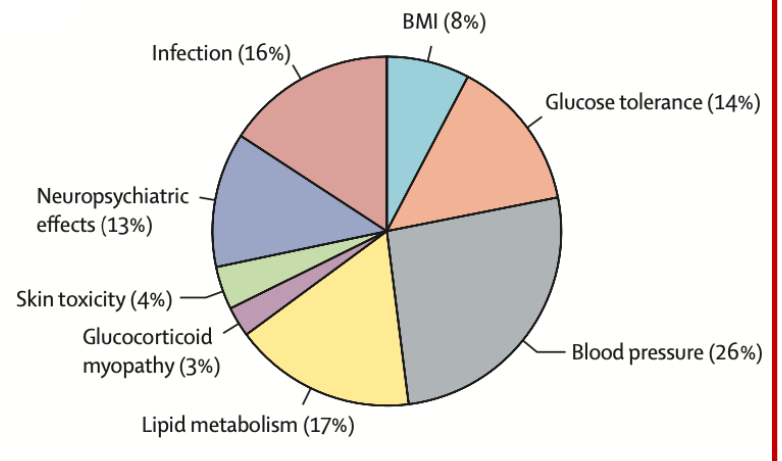
321 patients at week 13, 307 patients at week 26
Contribution to the overall CWS (by treatment arm)

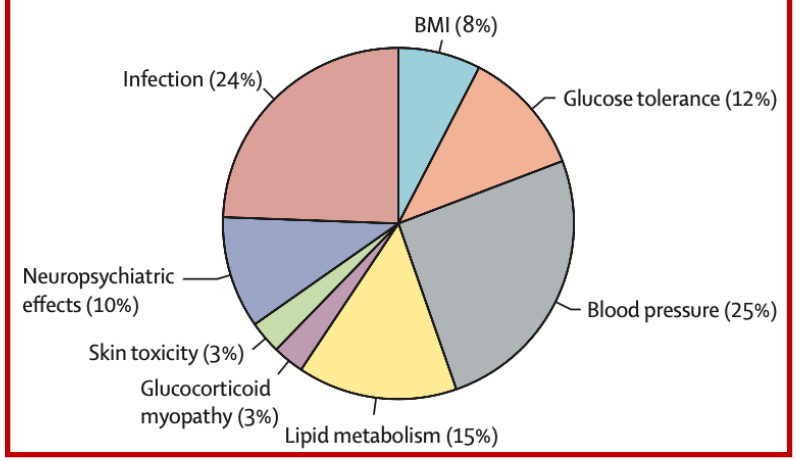
AVACOPAN





PREDNISONE





Patel NJ, et al. Lancet Rheumatol 2023; **5:**e130-38.

Was verstehen wir unter Co-Morbiditäten?

1987 *Charlson Comorbidity Index*

Disease	Points
Myocardial Infarction	1
Congestive Heart Failure	1
Peripheral Vascular disease	1
Cerebrovascular disease	1
Dementia	1
COPD	1
Connective Tissue disease	1
Peptic Ulcer disease	1
Diabetes Mellitus	1 point if uncomplicated 2 points if end-organ damage
Moderate to severe CKD	2
Hemiplegia	2
Leukaemia	2
Malignant Lymphoma	2
Solid Tumour	2 points 6 points if metastatic
Liver disease	1 point if mild 3 points if moderate to severe
AIDS	6 points

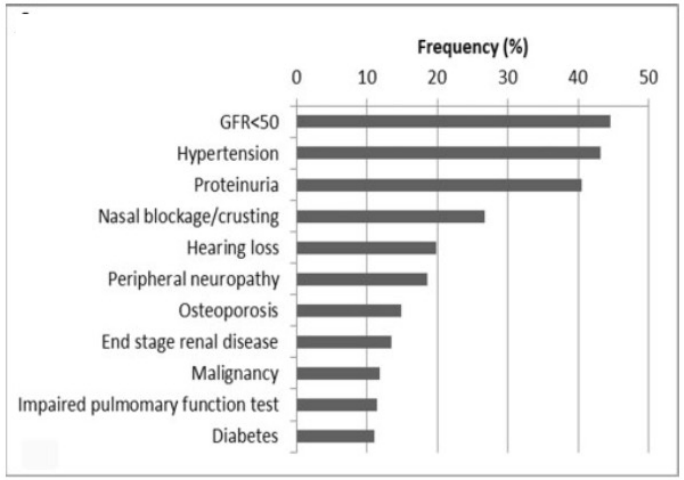
The potential interaction of e.g. diabetes on the diagnosis, treatment, or prognosis of a second disease

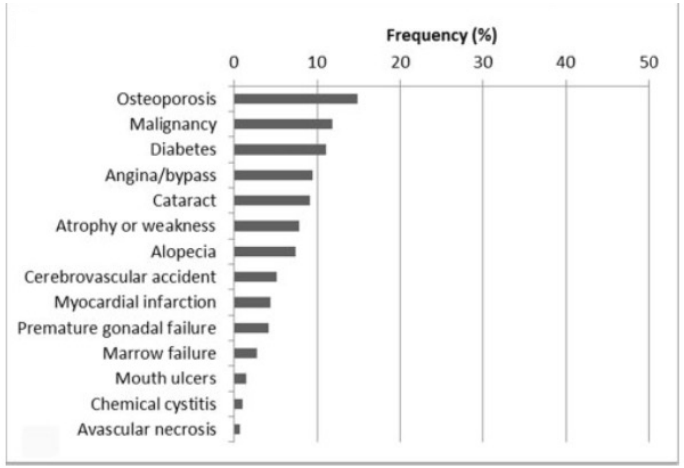
Impact on Clinical Activity	Examples
Diagnosis	
Made easier by coexisting disease	Most diabetic patients undergo regular fundus examinations, making the diagnosis of unrelated retinal disease, such as age-related macular retinopathy, more likely
Made more difficulty by a coexisting disease	Diabetic patients may have altered pain sensation, thereby interfering with and making more difficult the diagnosis of coronary heart disease
Treatment	
Indicated for existing and coexisting disease	Physical exercise as recommended for a patient with chronic obstructive pulmonary disease can have a beneficial effect on diabetes
Antagonistic effect on coexisting disease	Corticosteroids prescribed for chronic obstructive pulmonary disease in the same patient will have an antagonistic effect on the diabetes treatment
Prognosis	
Positively modified by a coexisting disease	Mortality associated with diabetes is increased in the presence of peripheral vascular disease
Not affected by a coexisting disease	Diabetes is unaffected by the presence of hypothyroidism

Molto A, et al. Clin Exp Rheumatol 2014; **32:**S-131-4.
Valderas JM, et al. Ann Fam Med 2009; **7:**357-363.

Welchen Einfluss haben Glukokortikoide auf Co-Morbiditäten?

Retrospective follow-up of trial patients over 7.3 years; frequency of most common VDI items and frequency of the 15 treatment-related damage items at LTFU



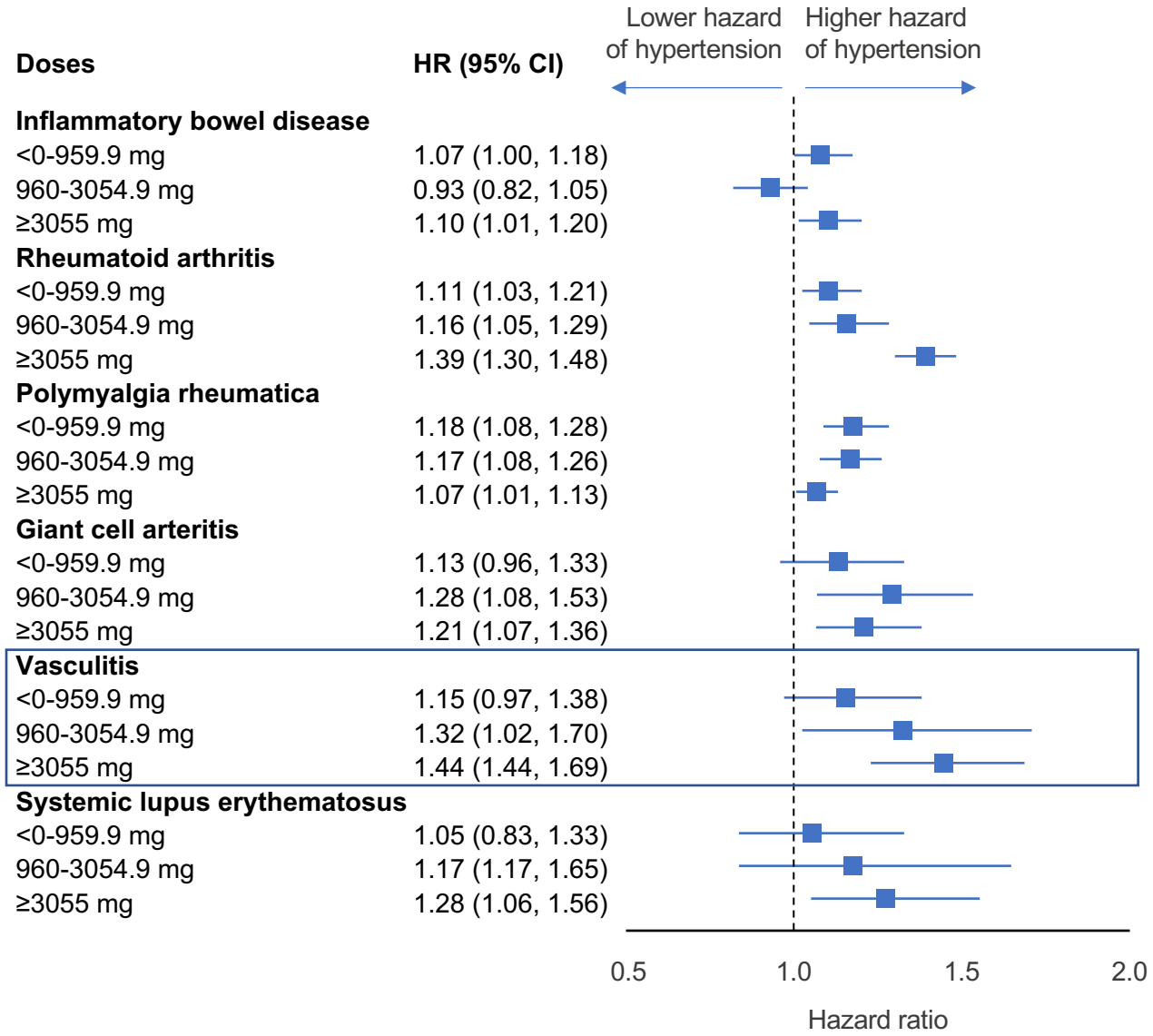


Estimated glomerular filtration rate at baseline, ≥4 relapses during follow-up and GC use (per 12 months) independently associated with high levels of damage at long-term follow-up

Factor	Number of items of damage at LTFU		High levels of damage at LTFU (VDI ⩾5)	
	β (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age at entry, per 10 years	0.242 (−0.001, 0.485)	0.051	1.125 (0.920, 1.375)	0.253
GFR at entry, per 10 ml/min	−0.110 (−0.216, −0.004)	0.041	0.844 (0.766, 0.930)	0.001
CRP at entry, per 10 mg/l	0.020 (0.001, 0.039)	0.041	1.018 (0.999, 1.038)	0.063
BVAS at entry, per 10 points	0.387 (0.006, 0.768)	0.046	1.207 (0.884, 1.648)	0.237
Four or more relapses during trial and follow-up	1.928 (0.358, 3.50)	0.016	7.582 (2.022, 28.43)	0.003
Glucocorticoid use, per 12 months	0.229 (−0.010, 0.468)	0.061	1.257 (1.033, 1.529)	0.022

Robson J, et al. Rheumatology 2015; **54:**471-481.

Welchen Einfluss haben Glukokortikoide auf Co-Morbiditäten?



71 642 patients (389 general practices); 40 648 received the diagnosis at study entry, while the others, on average, 5 years before study entry date

Median follow-up time was 6.5 years; and the incidence rate was 46.7/1000 person-years.

The rates of hypertension increased by increasing cumulative prednisolone-equivalent dose, by ***14%***, ***20%*** and ***30%*** when patients received between >0-959.9 mg, 960-3054.9 mg and ≥ 3055 mg

Mebrahtu TF, et al. CMAJ 2020; **192:**e295-E301.

Welchen Einfluss haben Glukokortikoide auf Co-Morbiditäten?

Daily dose (mg)†	Unadjusted HR (95% CI)	Adjusted* HR (95% CI)
None	1 (ref)	1 (ref)
1-<5	1.04 (0.61 to 1.76)	0.94 (0.55 to 1.59)
≥5–9	1.78 (1.35 to 2.35)	1.56 (1.18 to 2.05)
≥10	2.09 (1.44 to 3.05)	1.91 (1.31 to 2.79)
Cumulative dose (mg)†	**Unadjusted HR (95% CI)**	**Adjusted* HR (95% CI)**
Over preceding 6 months:		
None	1 (ref)	1 (ref)
1–380	0.93 (0.56 to 1.50)	0.86 (0.53 to 1.40)
381–750	1.31 (0.88 to 1.95)	1.20 (0.81 to 1.79)
751–1100	1.62 (1.18 to 2.24)	1.43 (1.04 to 1.98)
>1110	2.25 (1.57 to 3.22)	2.05 (1.42 to 2.94)
Over preceding 1 year:		
None	1 (ref)	1 (ref)
1–500	0.99 (0.64 to 1.54)	0.93 (0.60 to 1.45)
501–1100	1.28 (0.89 to 1.83)	1.19 (0.83 to 1.70)
1101–2100	1.63 (1.18 to 2.25)	1.47 (1.06 to 2.03)
>2100	1.97 (1.41 to 2.74)	1.74 (1.25 to 2.43)

19 902 patients with rheumatoid arthritis (CorEvitas registry)

1 106 CVE events occurred during a follow-up of 66 436 patient-years; yielding a rate of 1.66 CVE per 100 patient-years

Adjusted for age, sex, race, duration of RA, history of CV disease, diabetes mellitus, hyperlipidemia, hypertension, statin use, NSAID use, tobacco use, year of enrolment, baseline modified health assessment questionnaire score, CDAI and cs, b, tsDMARDs use

Ocon AJ, et al. Ann Rheum Dis 2021; **80:**1522-1529.

Fokus auf thrombotische Komplikationen

Summary of different studies reporting on VTE

	WGET							RAVE		
	Merkel	**Allenbach**	**Stassen**	**Novikov**	**Kronbichler**	**Kang**	**Berti**	**Kronbichler**	**Isaacs**	**Henry**
Participants	180	613	198	288	417	204	51	197	162	133
Frequency	8.9%	8.0% (GPA), 7.6% (MPA)	7.0% (GPA), 20.6% (MPA), 28.6% (RLV)	8.2% (GPA), 6.7% (MPA)	8.7% (GPA), 11.3% (MPA)	6.3% (GPA), 7.9% (MPA)	10.3%	9.5% (GPA), 4% (MPA)	16.8% (GPA), 10.7% (MPA)	17.8% (GPA), 17.0% (MPA)
Time to event (months)	2.07	5.8	8.8					1.5	1	3

Windpessl M, *et al*. Curr Rheum Rep 2021; **23:**37.

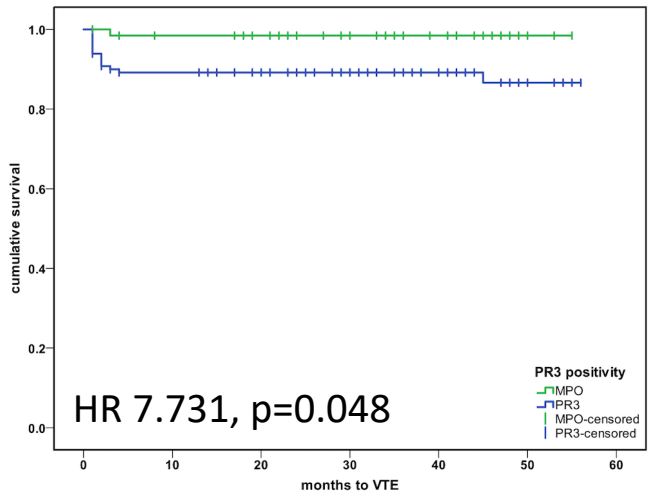
Fokus auf thrombotische Komplikationen

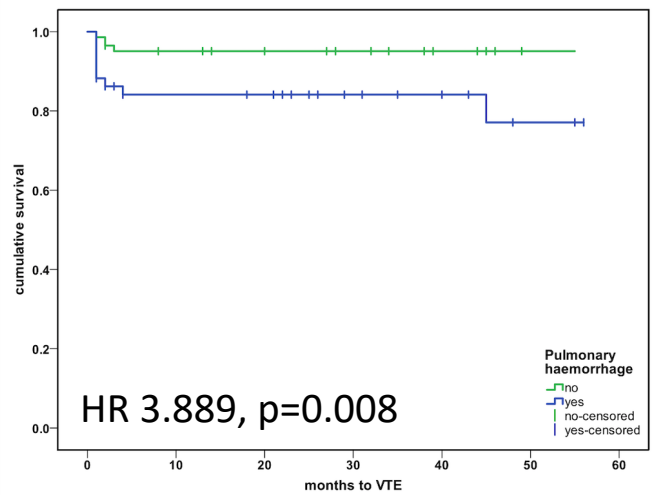
METHODS

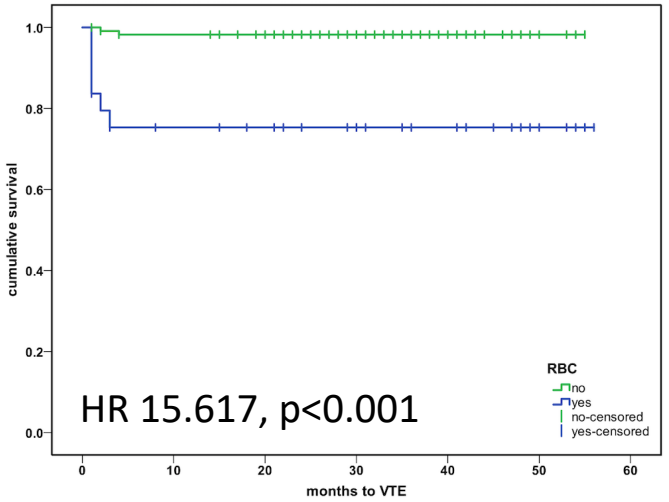
RAVE trial (Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis)
99 patients (Rituximab, 375 mg/m2 every week for four weeks)
98 patients (Cyclophophamide, adjusted per os, followed by azathioprine)

RESULTS

42/197 patients on any form of thromboprophylaxis
16 patients with VTE
Time from enrollment to VTE was 1.5 months







Kronbichler A, *et al*. Arthritis Rheumatol 2019; **71:**1888-1893.

Fokus auf thrombotische Komplikationen

International collaboration including 2 869 patients with AAV
VTE occurred in 9.7% of participants
Frequency similar across clinical phenotypes: 9.8%, 9.6% and 9.8% in GPA, MPA and EGPA

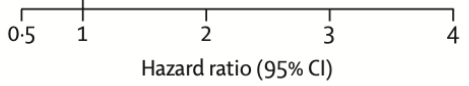
Variable	OR (95% CI)	*P*-value
Sex (male *vs* female)	1.32 (1.03, 1.69)	0.029
Age (per 1 year)	1.01 (0.99, 1.01)	0.265
PR3-ANCA *vs* MPO-ANCA	1.38 (1.03, 1.71)	0.029
Hypertension *vs* no hypertension	1.88 (1.21, 2.93)	0.005
Kidney function		
eGFR $\geq$60 ml/min/1.73 m^2	Reference	
eGFR 15–59 ml/min/1.73 m^2	1.75 (1.14, 2.68)	0.010
eGFR $\leq$14 ml/min/1.73 m^2	2.98 (1.97, 4.52)	0.001
CYC *vs* no CYC	1.60 (1.05, 2.43)	0.028
DEI skin *vs* no DEI skin	1.68 (1.07, 2.63)	0.025
DEI ENT *vs* no DEI ENT	0.61 (0.45, 0.84)	0.002
DEI chest *vs* no DEI chest	1.46 (1.02, 2.10)	0.040
DEI GI *vs* no DEI GI	1.13 (0.38, 3.31)	0.830
DEI renal *vs* no DEI renal	1.62 (1.05, 2.49)	0.028
DEI score at onset (per 1 point)	1.05 (1.00, 1.10)	0.032

Moiseev S, *et al*. Rheumatology 2021; **60:**4654-4661.

Fokus auf kardiovaskuläre Komplikationen

12 conditions: aortic aneurysm, AF, supraventricular arrhythmia, conduction system disease, HF, IHD, myocarditis/pericarditis, PAD, infective endocarditis, stroke/TIA, valve disorder, VTE

	Cohort		Events		Hazard ratio (95% CI)
	Autoimmune disease	Matched controls	Autoimmune disease	Matched controls	
Any autoimmune disease	446 449	2 102 830	68 413	231 410	1·56 (1·52–1·59)
Number of autoimmune diseases					
1	404 547	1 902 682	55 301	198 769	1·41 (1·37–1·45)
2	37 226	177 676	11 005	28 570	2·63 (2·49–2·78)
≥3	4676	22 472	2107	4071	3·79 (3·36–4·27)
Connective tissue diseases	160 217	761 918	36 846	118 391	1·68 (1·63–1·74)
Ankylosing spondylitis	9864	46 121	1423	3822	1·97 (1·65–2·35)
Polymyalgia rheumatica	48 102	231 802	15 390	55 870	1·47 (1·40–1·54)
Rheumatoid arthritis	66 796	318 456	15 520	46 594	1·83 (1·74–1·92)
Sjögren's syndrome	9933	47 330	2327	6139	2·08 (1·81–2·39)
Systemic lupus erythematosus	10 483	49 402	2204	4227	2·82 (2·38–3·33)
Systemic sclerosis	2159	10 310	752	1320	3·59 (2·81–4·59)
Vasculitis	37 940	178 494	7839	22 658	1·87 (1·73–2·01)



Conrad N, et al. Lancet 2022; **400:**733-743.

Fokus auf kardiovaskuläre Komplikationen

2. For ANCA-associated vasculitis the Framingham score may underestimate the CVR. Information from the European Vasculitis Society (EUVAS) model may supplement modifiable Framingham risk factors and is recommended to take into account. (LoE: 2b, GoR: D)

Risk score = -3.9 + (0.04*Age) – (0.95* PR3 ANCA) + (0.68*HTN)

Predicted risk of a cardiovascular event in 5 years = 1/ (1 + $e^{-\text{risk score}}$)

Drosos GC, *et al*. Ann Rheum Dis 2022

Suppiah R, *et al*. Arthritis Care Res 2011; **63:**588-96.

Fokus auf kardiovaskuläre Komplikationen

C. Patients with AAV should be periodically screened for treatment-related adverse effects and comorbidities. We recommend prophylaxis and lifestyle advice to reduce treatment-related complications and other comorbidities.

Statements 11, 13 and 15 of the 2016 update have been transferred to principle C. As the use of cyclophosphamide (CYC) is associated with an increased risk of bladder cancer,[27] all patients treated with CYC should have periodical urinalysis for the duration of their follow-up. In the presence of haematuria confirmed on urine microscopy that is not due to glomerulonephritis, a urology opinion must be sought. In common with other chronic inflammatory diseases, increased cardiovascular risk for patients with AAV is not explained by traditional risk factors alone and the risk of cardiovascular events is related to the burden of AAV disease activity.[28 29] Additionally, as a result of damage due to AAV and its treatment, the frequency of cardiovascular risk factors such as diabetes and hypertension is increased.[30] Therefore, both adequate control of vascular inflammation, and screening for and treatment of traditional cardiovascular risk factors, are important.[31] Screening for and management of other treatment-related and disease-related comorbidities, such as osteoporosis or chronic kidney disease, should also be conducted. While the available evidence is insufficient to recommend an AAV-specific evaluation of comorbidities, several EULAR and other recommendations[31–35] provide general guidance.

Annual (?) systematic assessment of risk factors:

- **Blood pressure:** resting blood pressure < 130 / 85 mmHg (SPRINT < 120 / 80 mmHg)

- **Reduction of salt intake**

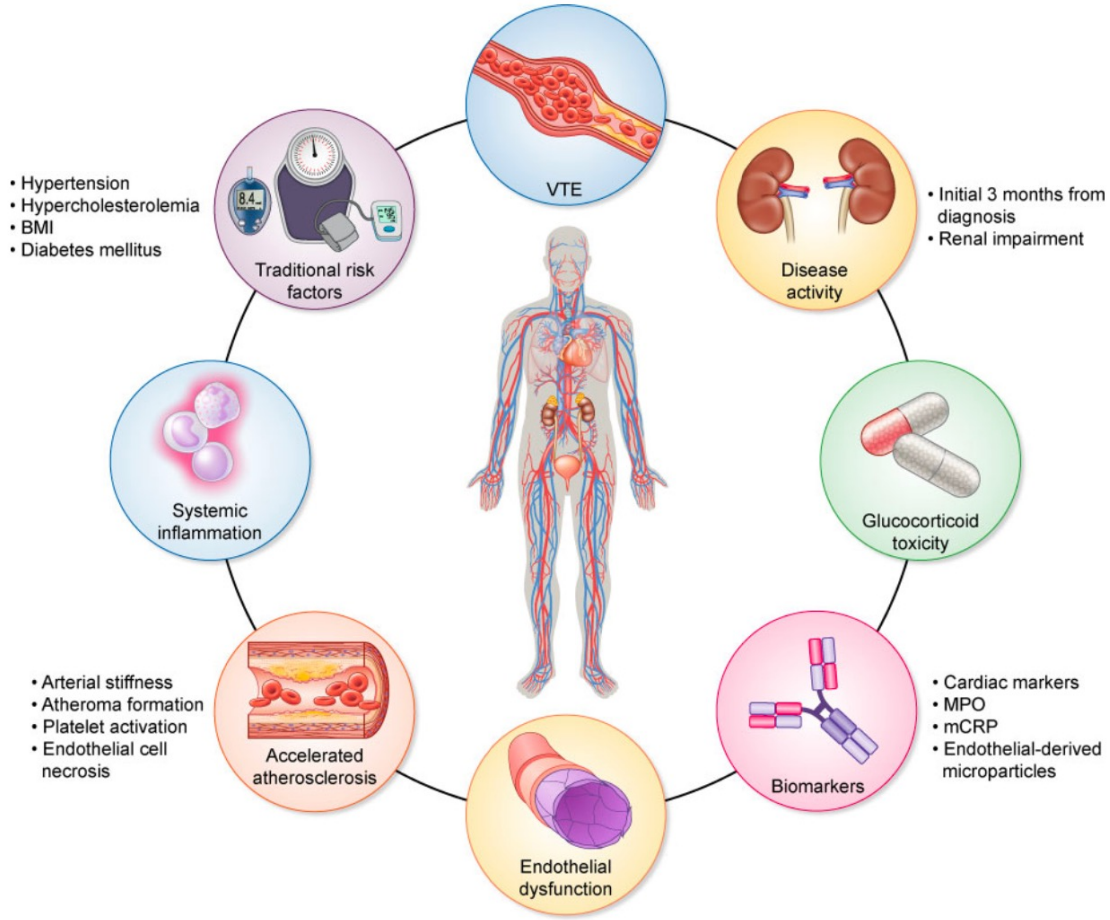
- **Cholesterol:**
  eGFR < 30 mL/min/1.73 m^2: LDL < 1.81 mmol/l
  all other patients: LDL < 2.59 mmol/l. (?)

- **Exercise**

- **Imaging** (i.e. echo?)

Hellmich B, et al. Ann Rheum Dis 2023; online ahead of print.

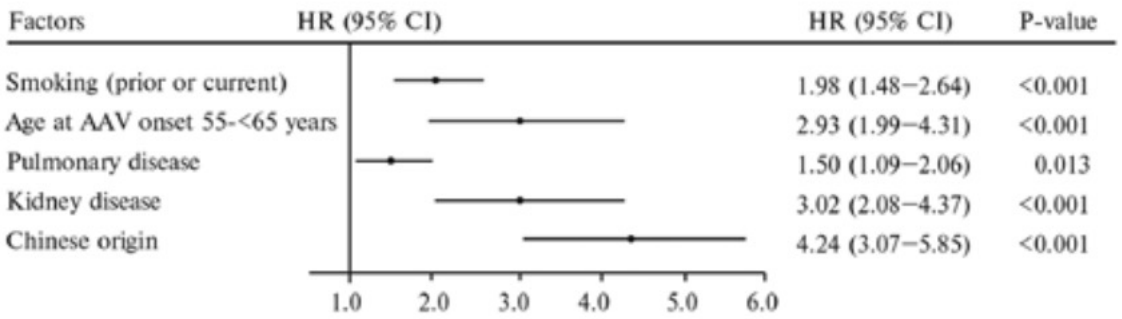
Fokus auf kardiovaskuläre Komplikationen



Floyd L, *et al*. Clin Kidney J 2022; **15:**618-623.

Fokus auf kardiovaskuläre Komplikationen

International collaboration including 2 286 patients with AAV
CVE occurred in 245 (10.7%) of participants
MI (8.1%) and stroke (3.2%), 0.6% presented with both
17.5 months from disease onset to CVE



Moiseev S, *et al*. J Rheumatol 2023; online ahead of print.

Fokus auf kardiovaskuläre Komplikationen

	Patients with recommendationn/N (%)	Guideline recommendation	Patients meeting recommendationn/N (%)
ESC/EAS Guidelines for Lipid Management in CVD[a]			
Very high CV risk	17/53 (32.1)	LDL-C < 70 mg/dl:	0/17 (2.8)
High CV risk	9/53 (17.0)	LDL-C < 100 mg/dl:	2/9 (22.2)
Moderate CV risk	14/53 (26.4)	LDL-C < 115 mg/dl:	2/14 (14.3)
Total	40/53 (75.5)		4/40 (10.0)
KDIGO Guidelines for Lipid Management in CKD[b,c]			
Adults aged ≥50 years and eGFR <60 ml/min.	27/51 (52.9)	Statins or statin + ezetimibe	6/27 (22.2)
Adults aged ≥50 years and eGFR ≥60 ml/min.	8/51 (15.7)	Statins	3/8 (37.5)
Adults aged 18–49 years with CKD and known CHD, prior ischemic stroke, diabetes mellitus, or estimated 10-year CV risk >10%	2/51 (3.9)	Statins	0/2 (0)
Total	37/51 (72.5)		9/37 (24.3)
KDIGO Guidelines for the Management of Blood Pressure in CKD[e]			
CKD and albumin excretion <30 mg/g Crea.	14/43 (32.6)	≤140/90 mmHg	11/14 (78.6)
CKD and albumin excretion >30 mg/g Crea.	20/43 (46.5)	≤130/80 mmHg	7/20 (35.0)
Total	34/43 (79.1)		18/34 (52.9)

Bramlage CP, *et al*. J Eval Clin Pract 2017; **23:**747-754.

Zusammenfassung

Glucocorticoid Toxicity Index: validated tool to measure the impact of GC exposure

Patients have an increased likelihood of disease- and treatment-related co-morbidities

Glucocorticoids increase the % of hypertension and cardiovascular events

Thromboembolic disease is present in a proportion of patients and correlate with active disease, but also severity of kidney disease

Cardiovascular risk management remains suboptimal and requires special attention to reduce the burden of cardiovascular events

Liste der Referenzen

Aqeel F, et al. Immune checkpoint inhibitors as potential triggers for ANCA vasculitis. RMD Open 2022;8:e002500.

Banik P et al. et al. Outcomes of Methotrexate as an Initial Induction and Maintenance Regimen for Localized Granulomatosis with Polyangiitis: A Retrospective Review. Arthritis Rheumatol 2022;74(suppl 9):Abstract #1082-ACR Convergence 2022

Benichou N, et al. Proteinuria and hematuria after remission induction are associated with outcome in ANCA-associated vasculitis. Kidney Int 2023. Epub ahead of print: doi: 10.1016/j.kint.2023.02.029.

Berden AE, et al. Histopathologic Classification of ANCA-Associated Glomerulonephritis. JASN 2010;21(10):1628-1636.

Berti A, et al. Autoreactive Plasmablasts After B Cell Depletion With Rituximab and Relapses in Antineutrophil Cytoplasmic Antibody–Associated Vasculitis. Arthitis Rheum 2023,75(5):736-747.

Bossuyt X, et al. Position paper: Revised 2017 international consensus on testing of ANCAs in granulomatosis with polyangiitis and microscopic polyangiitis. Nat Rev Rheumatol 2017;13(11):683–692.

Bramlage CP, et al. Management of cardiovascular risk factors in patients with ANCA-associated vasculitis. J Eval Clin Pract 2017;23:747-754.

Brix SR, et al. Development and validation of a renal risk score in ANCA-associated glomerulonephritis. Kidney Int 2018;94(6):1177-1188.

Charles P, et al. Comparison of individually tailored versus fixed-schedule rituximab regimen to maintain ANCA-associated vasculitis remission: results of a multicentre, randomised controlled, phase III trial (MAINRITSAN2). Ann Rheum Dis 2018;77:1443-1449.

Charles P, et al. Long-Term Rituximab Use to Maintain Remission of Antineutrophil Cytoplasmic Antibody–Associated Vasculitis. Ann Intern Med 2020;173(3):179–187.

Cohen Tervaert JW, et al. Prevention of relapses in Wegener's granulomatosis by treatment based on antineutrophil cytoplasmic antibody titre. Lancet 1990;336:709-711.

Conrad N, et al. Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK. Lancet 2022;400:733-743.

Corral-Gudino L, et al. Overall survival, renal survival and relapse in patients with microscopic polyangiitis: a systematic review of current evidence. Rheumatology (Oxford) 2011;50(8):1414-1423.

Cortazar FB, et al. Renal Recovery for Patients with ANCA-Associated Vasculitis and Low estimated GFR in the ADVOCATE Trial of Avacopan. Kidney Internat Reports 2023;8:860-870.

de Groot K, et al. Pulse versus daily oral cyclophosphamide for induction of remission in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized trial. Ann Intern Med 2009;150:670-680.

de Groot K, et al. Randomized trial of cyclophosphamide versus methotrexate for induction remission in early systemic antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Rheum 2005;52(8):2461-2469.

de Joode AAE, et al. Renal Survival in Proteinase 3 and Myeloperoxidase ANCA-Associated Systemic Vasculitis. Clin J Am Soc Nephrol 2013;8(10):1709-1717.

Delestre F, et al. Rituximab as Maintenance Therapy for ANCA-associated Vasculitides: Pooled Analysis and Long-term Outcome of MAINRITSAN Trials. Arthritis Rheumatol 2022;74(suppl 9):Abstract 0527-ACR Convergence 2022

Dendooven A, et al. Coding practice in national and regional kidney biopsy registries. BMC Nephrol 2021;22:193.

Diebold M, et al. Incidence of new onset glomerulonephritis after SARS-CoV-2 mRNA vaccination is not increased. Kidney Int. 2022;102(6):1409–1419.

Drosos GC, et al. EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome. Ann Rheum Dis 2022;81:768-779.

Egan AC, et al. The Sound of Interconnectivity; The European Vasculitis Society 2022 Report. Kidney Int Rep 2022;7(8):1745–1757.

Enghard P, et al. Imlifidase as novel treatment strategy in anti-neutrophil cytoplasmic antibody-induced pulmonary-renal syndrome. Kidney Int. 2021;100(6):1344-1345.

Flossmann O, et al. Long-term patient survival in ANCA-associated vasculitis. Ann Rheum Dis 2011;70(3):488–494.

Floyd L, et al. Cardiovascular disease and ANCA-associated vasculitis: are we missing a beat? Clin Kidney J 2022;15(4):618-623.

Floyd L, et al. Glucocorticoid Therapy in ANCA Vasculitis: Using the Glucocorticoid Toxicity Index as an Outcome Measure. Kidney360 2021;2(6):1002-1010.

Furuta S, et al. Effect of Reduced-Dose vs High-Dose Glucocorticoids Added to Rituximab on Remission Induction in ANCA-Associated Vasculitis: A Randomized Clinical Trial. JAMA 2021;325(21):2178-2187.

Gabilan C, et al. Avacopan as First-Line Treatment in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: A Steroid-Sparing Option. Kidney Int Rep 2022;7(5):1115-1118.

Gamerith G, et al. Association of baseline soluble immune checkpoints with the risk of relapse in PR3-ANCA vasculitis following induction of remission. Ann Rheum Dis 2023;82:253-261.

Geetha D, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis with renal involvement. J Am Soc Nephrol 2015;26(4):976-985.

Gercik O, et al. Histopathological subgrouping versus renal risk score for the prediction of end-stage renal disease in ANCA-associated vasculitis. Ann Rheum Dis 2020 May;79(5):675-676.

Grayson PC, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for Eosinophilic Granulomatosis with Polyangiitis. Ann Rheum Dis 2022;81(3):309-314.

Guillevin L, et al. Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. N Engl J Med 2014;371:1771-1780.

Hakroush S, B. Tampe. Tailored Use of Avacopan in a Case With Refractory Antineutrophil Cytoplasmic Antibody-Associated Renal Vasculitis and Concominant Complement System Activation. Kidney Int Rep 2022;8(2):376-378.

Hakroush S, et al. Bowman's capsule rupture links glomerular damage to tubulointerstitial inflammation in ANCA-associated glomerulonephritis. Clin Exp Rheumatol 2021;39 Suppl 129(2):27-31.

Hakroush S, et al. Histopathological Findings Predict Renal Recovery in Severe ANCA-Associated Vasculitis Requiring Intensive Care Treatment. Front Med 2022;7:622028.

Hakroush S, et al. Intrarenal synthesis of complement C3 localized to distinct vascular compartments in ANCA-associated renal vasculitis. J Autoimmun 2022;133:102924.

Hakroush S, Tampe B. Association between Loss of Immune Checkpoint Programmed Cell Death Protein 1 and Active ANCA-Associated Renal Vasculitis. Int J Mol Sci 2023,24(3),2975.

Hakroush S, Tampe B. Correspondence on ‘Bowman’s capsule rupture on renal biopsy improves the outcome prediction of ANCA-associated glomerulonephritis classifications’. Ann Rheum Dis 2019:http://dx.doi.org/10.1136/annrheumdis-2021-219970.

Liste der Referenzen

Hellmich B, et al. EULAR recommendations for conducting clinical studies and/or clinical trials in systemic vasculitis: focus on anti-neutrophil cytoplasm antibody-associated vasculitis. Ann Rheum Dis 2007;66(5):605–617.

Hellmich B, et al. EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. Ann Rheum Dis 2023;0:1–18. Epub ahead of print: doi:10.1136/ard-2022-223764

Holle JU, et al. Improved outcome in 445 patients with Wegener's granulomatosis in a German vasculitis center over four decades. Arthritis Rheum 2011;63(1):257-266

Iking-Konert C, et al. The Joint Vasculitis Registry in German-speaking countries (GeVas) - a prospective, multicenter registry for the follow-up of long-term outcomes in vasculitis. BMC Rheumatol 2021;5(1):40.

Jayne D, et al. A randomized trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies. N Engl J Med 2003;349:36-44.

Jayne D, et al. Avacopan for the Treatment of ANCA-Associated Vasculitis. N Engl J Med 2021;384(7):599–609.

Jayne D, et al. Randomized Trial of C5a Receptor Inhibitor Avacopan in ANCA-Associated Vasculitis. J Am. Soc Nephrol 2017;28(9):2756-2767.

Jayne DR, et al. Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. J Am Soc Nephrol 2007;18:2180-2188.

Jennette JC, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013;65(1):1–11.

Jones R, et al. Mycophenolate mofetil versus cyclophosphamide for remission induction in ANCA-associated vasculitis: a randomised, non-inferiority trial. Ann Rheum Dis 2019;78:399–405.

Jones RB, et al. ituximab versus cyclophosphamide in ANCA-associated renal vasculitis: 2-year results of a randomised trial. Ann Rheum Dis 2015;74:1178-1182.

Karras A, et al. Randomised controlled trial of prolonged treatment in the remission phase of ANCA-associated vasculitis. Ann Rheum Dis 2017;76(10):1662-1668.

Kauffmann M, et al. Disease Activity and Adverse Events in Patients with ANCA-Associated Vasculitides Undergoing Long-Term Dialysis. Clin J Am Soc Nephrol 2021;16(11):1665-1675.

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl 2013;3(1).

KDIGO 2023 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic antibody (ANCA)-Associated Vasculitis. Public Review Draft May 2023:https://kdigo.org/kdigo-2023-anca-guideline-update-available-for-public-review/

Kitching A, et al. ANCA-associated vasculitis. Nat Rev Dis Primers 2020;6(1):71.

Kronbichler A, et al. Classification criteria for ANCA-associated vasculitis: one size does not fit all! Rheumatology 2023;62(3):993-995.

Kronbichler A, et al. Clinical associations of renal involvement in ANCA-associated vasculitis. Autoimmun Rev 2020;19(4):102495.

Kronbichler A, et al. The Association of Pulmonary Haemorrhage, Positive PR3-ANCA and Urinary Red Blood Cell Casts with Venous Thromboembolism in ANCA-Associated Vasculitis. Arthritis Rheumatol 2019;71:1888-1893.

Kronbichler A, et al. Trimethoprim-sulfamethoxazole prophylaxis prevents severe/life-threatening infections following rituximab in antineutrophil cytoplasm antibody-associated vasculitis. Ann Rheum Dis 2018;77(10):1440-1447.

Lee T, et al. Predictors of treatment outcomes in ANCA-associated vasculitis with severe kidney failure. Clin J Am Soc Nephrol 2014;9(5):905-913.

Leeuwen J, et al. Biologics: Preliminary Assessment of Safety and Tolerability of Avacopan During the Early Access Program for ANCA-Associated Vasculitis. Targets and Therapy 2023;17:11–14.

Leeuwen J, et al. Compassionate Use of Avacopan in Difficult-to-Treat Antineutrophil Cytoplasmic Antibody–Associated Vasculitis. Kidney Int Rep 2021;7(3):624–628.

L'Imperio V, et al. Bowman's capsule rupture on renal biopsy improves the outcome prediction of ANCA-associated glomerulonephritis classifications. Ann Rheum Dis 2020:http://dx.doi.org/10.1136/annrheumdis-2020-217979.

Lyons PA, et al. Genetically distinct subsets within ANCA-associated vasculitis. N Engl J Med 2012;367(3):214-223.

Lyons PA, et al. Genome-wide association study of eosinophilic granulomatosis with polyangiitis reveals genomic loci stratified by ANCA status.Nat Commun 2019;10(1):5120.

Mahr A, et al. Subclassifying ANCA-associated vasculitis: a unifying view of disease spectrum. Rheumatology 2019;58(10):1707-1709.

Mansfield N, et al. Prolonged disease-free remission following rituximab and low-dose cyclophosphamide therapy for renal ANCA-associated vasculitis. Nephrol Dial Transplant 2011;26(10):3280-3286.

McClure M. B cell therapy in ANCA-associated vasculitis. Apollo 2022:https://doi.org/10.17863/CAM.86210

McClure ME, et al. Evaluation of PR3-ANCA Status After Rituximab for ANCA-Associated Vasculitis. J Clin Rheumatol 2019;25(5):217-223.

McGlinn K, et al. FAIRVASC: A semantic web approach to rare disease registry integration. Comput Biol Med 2022;145:105313.

McKinney EF, et al. T-cell exhaustion, co-stimulation and clinical outcome in autoimmunity and infection. Nature 2015;523(7562):612-616.

Mebrahtu TF, et al. Oral glucocorticoids and incidence of hypertension in people with chronic inflammatory diseases: a population-based cohort study. CMAJ 2020;192(12):e295-E301.

Merkel P, et al. Adjunctive Treatment With Avacopan, an Oral C5a Receptor Inhibitor, in Patients With Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. ACR Open Rheumatology 2020;2(11):662-671.

Miloslavsky E, et al. Development of a Glucocorticoid Toxicity Index (GTI) using multicriteria decision analysis. Ann Rheum Dis 2017;76(3): 543-546.

Moiseev S, et al. Association of venous thromboembolic events with skin, pulmonary and kidney involvement in ANCA-associated vasculitis: a multinational study. Rheumatology 2021;60:4654-4661.

Moiseev S, et al. Traditional and Disease Specific Risk Factors for Cardiovascular Events in ANCA-Associated Vasculitis: A Multinational Retrospective Study. J Rheumatol 2023; online ahead of print.

Moltó A, et al. Comorbidity indices. Clin Exp Rheumatol 2014;32(5 Suppl 85):S-131-4.

Moran SM, et al. The Clinical Application of Urine Soluble CD163 in ANCA-Associated Vasculitis. J Am Soc Nephrol 2021;32(11):2920-2932.

Moran SM, et al. Urinary soluble CD163 and monocyte chemoattractant protein-1 in the identification of subtle renal flare in anti-neutrophil cytoplasmic antibody-associated vasculitis. NDT 2020;35(2):283-291.

Morris AD, et al. Biomarkers in ANCA-Associated Vasculitis: Potential Pitfalls and Future Prospects. Kidney360 2021;2(3):586-597.

Liste der Referenzen

Moura MC, et al. Management of anti-neutrophil cytoplasmic antibody associated vasculitis with glomerulonephritis as proposed by the ACR 2021, EULAR 2022 and KDIGO 2021 Guidelines/Recommendations. Nephrol Dial Transplant 2023:gfad090.https://doi.org/10.1093/ndt/gfad090

Mukhtyar C, et al. EULAR recommendations for the management of primary small and medium vessel vasculitis. Ann Rheum Dis. 2008;68:310-317.

Ocon AJ, et al. Short-term dose and duration-dependent glucocorticoid risk for cardiovascular events in glucocorticoid-naive patients with rheumatoid arthritis. Ann Rheum Dis 2021;80(12):1522-1529.

Odler B, et al. Challenges of defining renal response in ANCA-associated vasculitis: call to action? Clin Kidney J 2023;sfad009, https://doi.org/10.1093/ckj/sfad009.

Odler B, et al. Risk factors for serious infections in ANCAassociated vasculitis. Ann Rheum Dis 2023,82(5):681-687.

O'Reilly VP, et al. Urinary Soluble CD163 in Active Renal Vasculitis. J Am Soc Nephrol 2016;27(9):2906-2916.

Ostendorf L, et al. Daratumumab for the treatment of refractory ANCA-associated vasculitis. RMD open 2023;9(1):e002742.

Patel N, et al. Glucocorticoid Toxicity Index scores by domain in patients with antineutrophil cytoplasmic antibody-associated vasculitis treated with avacopan versus standard prednisone taper: post-hoc analysis of data from the ADVOCATE trial. Lancet Rheumatol 2023;5:e130–38.

Person A, et al. In situ Visualization of C3/C5 Convertases to Differentiate Complement Activation. Kidney Int Rep 2022;5(6):927-930.

Pyo JY, et al. Reclassification of previously diagnosed GPA patients using the 2022 ACR/EULAR classification criteria. Rheumatology 2023;62(3):1179–1186.

Robson J, et al. Glucocorticoid treatment and damage in the anti-neutrophil cytoplasm antibody-associated vasculitides: long-term data from the European Vasculitis Study Group trials. Rheumatology 2015;54(3):471–481.

Robson JC, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for Granulomatosis With Polyangiitis. Arthritis Rheumatol 2022;74(3):393-399.

Rovin BH, et al. Executive summary of the KDIGO 2021 Guideline for the Management of Glomerular Diseases. Kidney Int 2021;100(4):753-779.

Sarica SH, et al. Multimorbidity in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: Results From a Longitudinal, Multicenter Data Linkage Study. Arthritis Rheumatol 2021;73(4):651-659.

Scurt FG, et al. ANCA-assoziierte Vaskulitis - Komplementfaktor C3 bestimmt den Krankheitsverlauf. DGIM 2023: Poster PS081.

Smith R, et al. Rituximab versus azathioprine for maintenance of remission for patients with ANCA-associated vasculitis and relapsing disease: an international randomised controlled trial. Ann Rheum Dis 2023:ard-2022-223559. Epub ahead of print. doi:10.1136/ard-2022-223559.

Smith RM, et al. Rituximab as therapy to induce remission after relapse in ANCA-associated vasculitis. Ann Rheum Dis 2020;79(9):1243–1249.

Solans-Laqué R, et al. Clinical characteristics and outcome of Spanish patients with ANCA-associated vasculitides: Impact of the vasculitis type, ANCA specificity, and treatment on mortality and morbidity. Medicine (Baltimore) 2017;96(8):e6083.

Stassen PM, et al. Induction of remission in active anti-neutrophil cytoplasmic antibody-associated vasculitis with mycophenolate mofetil in patients who cannot be treated with cyclophosphamide. Ann Rheum Dis 2007;66(6):798-802.

Stone JH, et al. Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis. N Engl J Med 2010;363(3):221–232.

Suppiah R, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for microscopic polyangiitis. Ann Reum Dis 2022;81(3):321-326.

Suppiah R, et al. A model to predict cardiovascular events in patients with newly diagnosed Wegener's granulomatosis and microscopic polyangiitis. Arthritis Care Res 2011; 63:588-596.

Takala JH, et al. Wegener's granulomatosis in Finland in 1981-2000: risk of dialysis-dependent renal disease. Scand J Rheumatol 2011;40(4):283-288.

Tam FWK, et al. Urinary monocyte chemoattractant protein-1 (MCP-1) is a marker of active renal vasculitis. NDT 2004;19(11):2761-2768.

Tampe D, et al. Low Serum Levels of Complement C3c at Diagnosis Indicate Poor Outcome in Antineutrophil Cytoplasmic Antibody-Associated Glomerulonephritis. Kidney Int Rep 2022;7(3):660-661.

Thietart S, et al. Evaluation of Rituximab for Induction and Maintenance Therapy in Patients 75 Years and Older With Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. JAMA Netw Open 2022;5(7):e2220925.

Uhlin F, et al. Endopeptidase Cleavage of Anti-Glomerular Basement Membrane Antibodies in vivo in Severe Kidney Disease: An Open-Label Phase 2a Study. JASN 2022;33(4):829-838.

Valderas JM, et al. Defining comorbidity: implications for understanding health and health services. Ann Fam Med 2009;7:357-363.

van Dam LS, et al. PR3-ANCAs predict relapses in ANCA-associated vasculitis patients after rituximab. NDT 2021;36(8):1408-1417.

van der Heijde D, et al. 2014 Update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. Ann Rheum Dis 2015;74(1):8-13.

Venhoff N, et al. Impact of Rituximab on Immunoglobulin Concentrations and B Cell Numbers after Cyclophosphamide Treatment in Patients with ANCA-Associated Vasculitides. PLOSone 2012;https://doi.org/10.1371/journal.pone.0037626.

Walsh M, et al. Plasma Exchange and Glucocorticoids in Severe ANCA-Associated Vasculitis. N Engl J Med 2020;382(7):622–631.

Walsh M, et al. The effects of plasma exchange in patients with ANCA-associated vasculitis: an updated systematic review and meta-analysis. BMJ 2022;376:e064604.

Watts RA, et al. Global epidemiology of vasculitis. Nat Rev Rheumatol 2022;18,22–34.

West BC, et al. Wegener Granulomatosis and Trimethoprim-Sulfamethoxazole. Complete remission after a twenty-year course. Ann Int Med 1987;106(6):840-842.

Windpessl M, et al. ANCA Status or Clinical Phenotype - What Counts More? Curr Rheum Rep 2021;23(6):37.

Xiao H, et al. C5a receptor (CD88) blockade protects against MPO-ANCA GN. J Am Soc Nephrol 2014;25(2):225-231.

Yates M, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis 2016;75(9):1583–1594.

Zipfel PF, et al. Complement catalyzing glomerular diseases. Cell Tissue Res 2021;385:355–370.

Zipfel PF, et al. Complement Inhibitors in Clinical Trials for Glomerular Diseases. Frontiers Immunol 2019;10:2166.

Die Fachpersonen können bei Vifor Pharma Switzerland AG eine vollständige Kopie des zitierten Prüfungsberichts anfordern.

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TAVNEOS®▼ 10 mg Hartkapseln: Wirkstoff: Avacopan. **Zusammensetzung:** Jede Hartkapsel enthält 10 mg Avacopan. Sonstige Bestandteile mit bekannter Wirkung: 245 mg Macrogolglycerolhydroxystearat (Ph.Eur.). **Anwendungsgebiete:** Tavneos ist in Kombination mit einem Rituximab- oder Cyclophosphamid-Dosierungsschema indiziert zur Behandlung erwachsener Patienten mit schwerer aktiver Granulomatose mit Polyangiitis (GPA) oder mikroskopischer Polyangiitis (MPA). **Gegenanzeigen:** Überempfindlichkeit gegen den Wirkstoff oder einen der sonstigen Bestandteile. **Nebenwirkungen:** Sehr häufig: Übelkeit, Kopfschmerzen, erniedrigte Leukozytenzahl, Infektion der oberen Atemwege, Diarrhö, Erbrechen, Nasopharyngitis, erhöhte Werte in Leberfunktionstests. Häufig: Pneumonie, Rhinitis, Harnwegsinfektion, Sinusitis, Bronchitis, Gastroenteritis, Infektion der unteren Atemwege, Zellulitis, Herpes zoster, Influenza, Orale Candidose, Oraler Herpes, Otitis media, Neutropenie, Schmerzen im Oberbauch, erhöhte Kreatinphosphokinase im Blut. Gelegentlich: Angioödem. **VERSCHREIBUNGSPFLICHTIG. Fachinformation beachten. Pharmazeutischer Unternehmer:** Vifor Fresenius Medical Care Renal Pharma France, 100-101 Terrasse Boieldieu, Tour Franklin La Défense 8, 92042 Paris La Défense Cedex, Frankreich. **Stand der Information:** Februar 2022

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Schweiz

▼Dieses Arzneimittel unterliegt einer zusätzlichen Überwachung. Für weitere Informationen, siehe Fachinformation TAVNEOS® auf www.swissmedicinfo.ch.

Tavneos®: Z: Avacopan. **I:** Tavneos, als ergänzende Therapie zu einer immunsuppressiven Standardbehandlung auf Basis von Rituximab oder Cyclophosphamid mit Glukokortikoiden, ist für die Behandlung erwachsener Patienten mit schwerer aktiver ANCA Vaskulitis (GPA/MPA) indiziert. **D:** Orale Einnahme morgens und abends 2x täglich 30 mg (3 Kapseln zu je 10 mg) mit Nahrung. **KI:** Überempfindlichkeit gegen den Wirkstoff oder einen der Hilfsstoffe. **VM:** Hepatotoxizität; Angioödem; Überwachung des Blutbildes (weisse Blutkörperchen); Schwere Infektionen; Reaktivierung des Hepatitis-B-Virus; Herzbeschwerden; Bösartige Tumore; Macroglycerinhydroxystearat. **S/S:** Eine Anwendung während der Schwangerschaft und bei Frauen im gebärfähigen Alter, die keine Verhütungsmethode anwenden, ist nicht empfohlen. Es ist nicht bekannt, ob Avacopan in die Muttermilch ausgeschieden wird. Der Nutzen des Stillens für das Kind sollte gegen den Nutzen der Behandlung für die Patientin abgewogen werden. **UW:** Sehr häufig: Infektion der oberen Atemwege, Nasopharyngitis; Kopfschmerzen; Erbrechen, Durchfall, Übelkeit; erhöhter Lebertest; verminderte Anzahl weisser Blutkörperchen. Häufig: Lungenentzündung, Infektion der unteren Atemwege, Influenza, Bronchitis, Zellulitis, Infektion der Harnwege, Herpes zoster, Sinusitis, orale Candidose, Herpes im Mundbereich, Otitis media, Rhinitis, Gastroenteritis; Neutropenie; Oberbauchschmerzen; Anstieg der Kreatinphosphokinase im Blut. Gelegentlich: Angioödeme. **IA:** Avacopan ist ein Substrat von CYP3A4. Die gleichzeitige Verabreichung von Induktoren oder Inhibitoren dieses Enzyms kann die Pharmakokinetik von Avacopan beeinflussen. Siehe Fachinformation. **P:** Tavneos 10 mg: 30 und 180 Hartkapseln. **Liste B**. Detaillierte Informationen**:** www.swissmedicinfo.ch. Stand der Information**:** September 2022. **Zulassungsinhaberin:** Vifor Fresenius Medical Care Renal Pharma Ltd., St. Gallen. **Vertrieb:** Vifor Pharma Switzerland AG, CH-1752 Villars-sur-Glâne | CH-AVA-2300011